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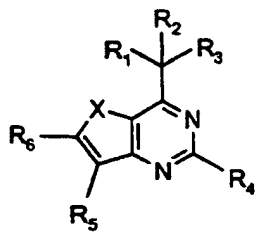

(I)

(57) Abstract: A compound of formula (I) wherein X is O or S; R_1 and R_2 are independently selected from hydrogen, alkyl, aryl, hydroxy, alkoxy, aryloxy, cyano, nitro, CO_2R_7, COR_7, $OCOR_7CONR_7R_8$, $CONR_7NR_8R_9$, $OCONR_7R_8$, NR_7R_8, NR_7COR_8, $NR_7CONR_8R_9$, $NR_7CO_2R_8$, $NR_7SO_2R_8$, $NR_7CONR_8NR_9R_{10}$, $NR_7NR_8CO_2R_9$, $NR_7NR_8CONR_9R_{10}$, $NR_7SO_2NR_8R_9$, SO_2R_7, SOR_7, SR_7 and $SO_2NR_7R_8$, or R_1 and R_2 together form a carbonyl group (C=O), an oxime group ($C=NOR_{11}$), an imine group ($C=NR_{11}$) or a hydrazone group ($C=NNR_{11}R_{12}$), or R_1 and R_2 together form a 5, 6 or 7 membered carbocyclic or heterocyclic ring; R_3 is alkyl or aryl; R_4, R_5 and R_6 are independently selected from hydrogen, alkyl, aryl, halogen, hydroxy, nitro, cyano, alkoxy, aryloxy, COR_7, $OCOR_7$, CO_2R_7, SR_7, SOR_7, SO_2R_7, $SO_2NR_7R_8$, $CONR_7R_8$, $CONR_7NR_8R_9$, $OCONR_7R_8$, NR_7R_8, NR_7COR_8, $NR_7CONR_8R_9$, $NR_7CO_2R_8$, $NR_7SO_2R_8$, $CR_7{=}NOR_8$, $NR_7CONR_8NR_9R_{10}$, $NR_7NR_8CO_2R_9$, $NR_7NR_8CONR_9R_{10}$, $SO_2NR_7NR_8R_9$, $NR_7SO_2NR_8R_9$, $NR_7NR_8SO_2R_9$, $NR_7NR_8COR_9$, $NR_7NR_8R_9$ and $NR_7CSNR_8R_9$, or R_5 and R_6 together form a 5, 6 or 7 membered carbocyclic or heterocyclic ring; and R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are independently selected from hydrogen, alkyl and aryl, or a pharmaceutically acceptable salt thereof or prodrug thereof, and the use thereof in therapy, particularly in the therapy of a disorder in which the blocking of purine receptors may be beneficial, such as Parkinson's Disease.

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THIENO- AND FUROPYRIMIDINE DERIVATIVES AS A2A-RECEPTOR ANTAGONISTS

The present invention relates to novel thieno[3,2-d]pyrimidine and furo[3,2-d]pyrimidine derivatives and their use in therapy. In particular, the present invention relates to the treatment of disorders in which the reduction of purinergic neurotransmission could be beneficial. The invention relates in particular to adenosine receptors and particularly adenosine A_{2A} receptors, and to the treatment of movement disorders such as Parkinson's disease.

Movement disorders constitute a serious health problem, especially amongst the elderly sector of the population. These movement disorders are often the result of brain lesions. Disorders involving the basal ganglia which result in movement disorders include Parkinson's disease, Alzheimer's disease, Huntington's chorea and Wilson's disease. Furthermore, dyskinesias often arise as sequelae of cerebral ischaemia and other neurological disorders.

There are four classic symptoms of Parkinson's disease: tremor, rigidity, akinesia and postural changes. The disease is also commonly associated with depression, dementia and overall cognitive decline. Parkinson's disease has a prevalence of 1 per 1,000 of the total population. The incidence increases to 1 per 100 for those aged over 60 years. Degeneration of dopaminergic neurones in the substantia nigra and the subsequent reductions in interstitial concentrations of dopamine in the striatum are critical to the development of Parkinson's disease. Some 80% of cells from the substantia nigra need to be destroyed before the clinical symptoms of Parkinson's disease are manifested.

Current strategies for the treatment of Parkinson's disease are based on transmitter replacement therapy (L-dihydroxyphenylacetic acid (L-DOPA)), inhibition of monoamine oxidase (e.g. Deprenyl®), dopamine receptor agonists (e.g. bromocriptine and apomorphine) and anticholinergics (e.g. benztrophine, orphenadrine). Transmitter replacement therapy in particular does not provide consistent clinical benefit, especially after prolonged treatment when "on-off" symptoms develop, and this treatment has also been associated with involuntary movements of athetosis and chorea, nausea and vomiting. Additionally current therapies do not treat the underlying neurodegenerative disorder

resulting in a continuing cognitive decline in patients. Despite new drug approvals, there is still a medical need in terms of improved therapies for movement disorders, especially Parkinson's disease. In particular, effective treatments requiring less frequent dosing, effective treatments which are associated with less severe side-effects, and effective treatments which control or reverse the underlying neurodegenerative disorder, are required.

Blockade of A_2 adenosine receptors has recently been implicated in the treatment of movement disorders such as Parkinson's disease (Richardson, P.J. *et al.*, *Trends Pharmacol. Sci.* 1997, 18, 338-344) and in the treatment of cerebral ischaemia (Gao, Y. and Phillis, J.W., *Life Sci.* 1994, 55, 61-65). The potential utility of adenosine A_{2A} receptor antagonists in the treatment of movement disorders such as Parkinson's Disease has recently been reviewed (Mally, J. and Stone, T.W., *CNS Drugs*, 1998, 10, 311-320).

Adenosine is a naturally occurring purine nucleoside which has a wide variety of well-documented regulatory functions and physiological effects. The central nervous system (CNS) effects of this endogenous nucleoside have attracted particular attention in drug discovery, owing to the therapeutic potential of purinergic agents in CNS disorders (Jacobson, K.A. *et al.*, *J. Med. Chem.* 1992, 35, 407-422). This therapeutic potential has resulted in considerable recent research endeavour within the field of adenosine receptor agonists and antagonists (Bhagwhat, S.S.; Williams, M. *Exp. Opin. Ther. Patents* 1995, 5,547-558).

Adenosine receptors represent a subclass (P_1) of the group of purine nucleotide and nucleoside receptors known as purinoreceptors. The main pharmacologically distinct adenosine receptor subtypes are known as A_1, A_{2A}, A_{2B} (of high and low affinity) and A_3 (Fredholm, B.B., *et al.*, *Pharmacol. Rev.* 1994, 46, 143-156). The adenosine receptors are present in the CNS (Fredholm, B.B., *News Physiol. Sci.*, 1995, 10, 122-128).

The design of P_1 receptor-mediated agents has been reviewed (Jacobson, K.A., Suzuki, F., *Drug Dev. Res.*, 1997, 39, 289-300; Baraldi, P.G. *et al.*, *Curr. Med. Chem.* 1995, 2, 707-722), and such compounds are claimed to be useful in the treatment of cerebral ischemia or neurodegenerative disorders, such as Parkinson's disease (Williams, M. and Burnstock, G.

Purinergic Approaches Exp. Ther. (1997), 3-26. Editor: Jacobson, Kenneth A.; Jarvis, Michael F. Publisher: Wiley-Liss, New York, N.Y.)

The pharmacology of adenosine A_{2A} receptors has been reviewed (Ongini, E.; Fredholm, B.B. *Trends Pharmacol. Sci.* 1996, 17(10), 364-372). One potential underlying mechanism in the aforementioned treatment of movement disorders by the blockade of A_2 adenosine receptors is the evidence of a functional link between adenosine A_{2A} receptors to dopamine D_2 receptors in the CNS. Some of the early studies (e.g. Ferre, S. *et al.*, Stimulation of high-affinity adenosine A_2 receptors decreases the affinity of dopamine D_2 receptors in rat striatal membranes. *Proc. Natl. Acad. Sci.* U.S.A. 1991, 88, 7238-41) have been summarised in two more recent articles (Fuxe, K. *et al., Adenosine Adenine Nucleotides Mol. Biol. Integr. Physiol.*, [Proc. Int. Symp.], 5th (1995), 499-507. Editors: Belardinelli, Luiz; Pelleg, Amir. Publisher: Kluwer, Boston, Mass.; Ferre, S. *et al., Trends Neurosci.* 1997, 20, 482-487).

As a result of these investigations into the functional role of adenosine A_{2A} receptors in the CNS, especially *in vivo* studies linking A_2 receptors with catalepsy (Ferre *et al., Neurosci. Lett.* 1991, 130, 162-4; Mandhane, S.N. *et al., Eur. J. Pharmacol.* 1997, 328, 135-141) investigations have been made into agents which selectively bind to adenosine A_{2A} receptors as potentially effective treatments for Parkinson's disease.

While many of the potential drugs for treatment of Parkinson's disease have shown benefit in the treatment of movement disorders, an advantage of adenosine A_{2A} antagonist therapy is that the underlying neurodegenerative disorder may also be treated. The neuroprotective effect of adenosine A_{2A} antagonists has been reviewed (Ongini, E.; Adami, M.; Ferri, C.; Bertorelli, R., *Ann. N. Y. Acad. Sci.* 1997, 825(Neuroprotective Agents), 30-48).

Xanthine derivatives have been disclosed as adenosine A_2 receptor antagonists as useful for treating various diseases caused by hyperfunctioning of adenosine A_2 receptors, such as Parkinson's disease (see, for example, EP-A-565377).

One prominent xanthine-derived adenosine A_{2A} selective antagonist is CSC [8-(3-chlorostyryl)caffeine] (Jacobson *et al., FEBS Lett.*, 1993, 323, 141-144).

Theophylline (1,3-dimethylxanthine), a bronchodilator drug which is a mixed antagonist at adenosine A_1 and A_{2A} receptors, has been studied clinically. To determine whether a formulation of this adenosine receptor antagonist would be of value in Parkinson's disease an open trial was conducted on 15 Parkinsonian patients, treated for up to 12 weeks with a slow release oral theophylline preparation (150 mg/day), yielding serum theophylline levels of 4.44 mg/L after one week. The patients exhibited significant improvements in mean objective disability scores and 11 reported moderate or marked subjective improvement (Mally, J., Stone, T.W. *J. Pharm. Pharmacol.* 1994, 46, 515-517).

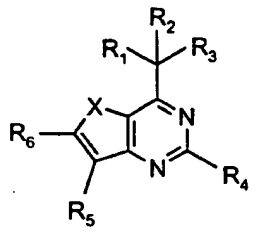
KF 17837 [(E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine] is a selective adenosine A_{2A} receptor antagonist which on oral administration significantly ameliorated the cataleptic responses induced by intracerebroventricular administration of an adenosine A_{2A} receptor agonist, CGS 21680. KF 17837 also reduced the catalepsy induced by haloperidol and reserpine. Moreover, KF 17837 potentiated the anticataleptic effects of a subthreshold dose of L-DOPA plus benserazide, suggesting that KF 17837 is a centrally active adenosine A_{2A} receptor antagonist and that the dopaminergic function of the nigrostriatal pathway is potentiated by adenosine A_{2A} receptor antagonists (Kanda, T. *et al.*, *Eur. J. Pharmacol.* 1994, 256, 263-268). The structure activity relationship (SAR) of KF 17837 has been published (Shimada, J. *et al.*, *Bioorg. Med. Chem. Lett.* 1997, 7, 2349-2352). Recent data has also been provided on the A_{2A} receptor antagonist KW-6002 (Kuwana, Y *et al.*, *Soc. Neurosci. Abstr.* 1997, 23, 119.14; and Kanda, T. *et al.*, *Ann. Neurol.* 1998, 43(4), 507-513).

New non-xanthine structures sharing these pharmacological properties include SCH 58261 and its derivatives (Baraldi, P.G. *et al.*, Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine Derivatives: Potent and Selective A_{2A} Adenosine Antagonists. *J. Med. Chem.* 1996, 39, 1164-71). SCH 58261 (7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-[4,3-e]-1,2,4-triazolo[1,5-c] pyrimidine) is reported as effective in the treatment of movement disorders (Ongini, E. *Drug Dev. Res.* 1997, 42(2), 63-70) and has been followed up by a later series of compounds (Baraldi, P.G. *et al.*, *J. Med. Chem.* 1998, 41(12), 2126-2133).

The foregoing discussion indicates that a potentially effective treatment for movement disorders in humans would comprise agents which act as antagonists at adenosine A_{2A} receptors.

It has now been found that novel thieno[3,2-d]pyrimidine and furo[3,2-d]pyrimidine derivatives, which are structurally unrelated to known adenosine receptor antagonists, exhibit unexpected antagonist binding affinity at adenosine (P_1) receptors, and in particular at the adenosine A_{2A} receptor. Such compounds may therefore be useful for the treatment of disorders in which the blocking of purine receptors, particularly adenosine receptors and more particularly adenosine A_{2A} receptors, may be beneficial. In particular such compounds may be suitable for the treatment of movement disorders, such as disorders of the basal ganglia which result in dyskinesias. These may include Parkinson's disease, Alzheimer's disease, spasticity, Huntington's chorea and Wilson's disease.

According to the present invention there is provided a compound of formula (I):



I

wherein:

X is O or S;

R_1 and R_2 are independently selected from hydrogen, alkyl, aryl, hydroxy, alkoxy, aryloxy, cyano, nitro, CO_2R_7, COR_7, $OCOR_7$, $CONR_7R_8$, $CONR_7NR_8R_9$, $OCONR_7R_8$, NR_7R_8, NR_7COR_8, $NR_7CONR_8R_9$, $NR_7CO_2R_8$, $NR_7SO_2R_8$, $NR_7CONR_8NR_9R_{10}$, $NR_7NR_8CO_2R_9$, $NR_7NR_8CONR_9R_{10}$, $NR_7SO_2NR_8R_9$, SO_2R_7, SOR_7, SR_7 and $SO_2NR_7R_8$, or R_1 and R_2 together form a carbonyl group (C=O), an oxime group (C=NOR$_{11}$), an imine group (C=NR$_{11}$) or a hydrazone group (C=NNR$_{11}$R$_{12}$), or R_1 and R_2 together form a 5, 6 or 7 membered carbocyclic or heterocyclic ring;

R_3 is alkyl or aryl;

R_4, R_5 and R_6 are independently selected from hydrogen, alkyl, aryl, halogen, hydroxy, nitro, cyano, alkoxy, aryloxy, COR_7, $OCOR_7$, CO_2R_7, SR_7, SOR_7, SO_2R_7,

$SO_2NR_7R_8$, $CONR_7R_8$, $CONR_7NR_8R_9$, $OCONR_7R_8$, NR_7R_8, NR_7COR_8, $NR_7CONR_8R_9$, $NR_7CO_2R_8$, $NR_7SO_2R_8$, $CR_7{=}NOR_8$, $NR_7CONR_8NR_9R_{10}$, $NR_7NR_8CO_2R_9$, $NR_7NR_8CONR_9R_{10}$, $SO_2NR_7NR_8R_9$, $NR_7SO_2NR_8R_9$, $NR_7NR_8SO_2R_9$, $NR_7NR_8COR_9$, $NR_7NR_8R_9$ and $NR_7CSNR_8R_9$, or R_5 and R_6 together form a 5, 6 or 7 membered carbocyclic or heterocyclic ring; and

R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are independently selected from hydrogen, alkyl and aryl,

or a pharmaceutically acceptable salt thereof or prodrug thereof.

As used herein, the term "alkyl" means a branched or unbranched, cyclic or acyclic, saturated or unsaturated (e.g. alkenyl or alkynyl) hydrocarbyl radical which may be substituted or unsubstituted. Where cyclic, the alkyl group is preferably C_3 to C_{12}, more preferably C_5 to C_{10}, more preferably C_5, C_6 or C_7. Where acyclic, the alkyl group is preferably C_1 to C_{10}, more preferably C_1 to C_6, more preferably methyl, ethyl, propyl (n-propyl or isopropyl), butyl (n-butyl, isobutyl or tertiary-butyl) or pentyl (including n-pentyl and iso-pentyl), more preferably methyl. It will be appreciated therefore that the term "alkyl" as used herein includes alkyl (branched or unbranched), alkenyl (branched or unbranched), alkynyl (branched or unbranched), cycloalkyl, cycloalkenyl and cycloalkynyl.

As used herein, the term "lower alkyl" means methyl, ethyl, propyl (n-propyl or isopropyl) or butyl (n-butyl, isobutyl or tertiary-butyl).

As used herein, the term "aryl" means an aromatic group, such as phenyl or naphthyl, or a heteroaromatic group containing one or more heteroatom, such as pyridyl, pyrrolyl, quinolinyl, furanyl, thienyl, oxadiazolyl, thiadiazolyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, imidazolyl or pyrimidinyl.

As used herein, the term "alkoxy" means alkyl-O-. As used herein, the term "aryloxy" means aryl-O-.

As used herein, the term "halogen" means a fluorine, chlorine, bromine or iodine radical.

As used herein the term "R_1 and R_2 together form a carbonyl group, an oxime group, an imine group or a hydrazone group" means that R_1 and R_2 in combination with the carbon atom to which they are bound together form a carbonyl group, an oxime group, an imine group or a

hydrazone group, i.e. the carbon atom to which R_1 and R_2 are bound in formula (I) is attached via a double bond to an oxygen atom (for compounds wherein R_1 and R_2 together form a carbonyl group) or to a nitrogen atom (for compounds wherein R_1 and R_2 together form an oxime, imine or hydrazone group).

As used herein the term "oxime group" means a group of formula $C = N - OR_{11}$ where R_{11} is selected from hydrogen, alkyl and aryl.

As used herein the term "imine group" means a group of formula $C = N - R_{11}$ where R_{11} is selected from hydrogen, alkyl and aryl.

As used herein the term "hydrazone group" means a group of formula $C=N-NR_{11}R_{12}$ where R_{11} and R_{12} are independently selected from hydrogen, alkyl and aryl.

As used herein, the term "prodrug" means any pharmaceutically acceptable prodrug of a compound of the present invention.

According to the first embodiment of the invention, alkyl and aryl groups may be substituted or unsubstituted. Where substituted, there will generally be 1 to 3 substituents present, preferably 1 substituent. According to the first embodiment of the invention, substituents may include:

carbon-containing groups such as

alkyl,	
aryl,	(e.g. substituted and unsubstituted phenyl),
arylalkyl;	(e.g. substituted and unsubstituted benzyl);

halogen atoms and halogen containing groups such as

haloalkyl	(e.g. trifluoromethyl),
haloaryl	(e.g. chlorophenyl);

oxygen containing groups such as

alcohols	(e.g. hydroxy, hydroxyalkyl, hydroxyaryl, (aryl)(hydroxy)alkyl),
ethers	(e.g. alkoxy, aryloxy, alkoxyalkyl, aryloxyalkyl, alkoxyaryl, aryloxyaryl),

aldehydes (e.g. carboxaldehyde),

ketones (e.g. alkylcarbonyl, arylcarbonyl, alkylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylalkyl, arylcarbonylaryl, arylalkylcarbonyl, arylalkylcarbonylalkyl, arylalkylcarbonylaryl)

acids (e.g. carboxy, carboxyalkyl, carboxyaryl),

acid derivatives such as esters (e.g. alkoxycarbonyl, aryloxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, alkylcarbonyloxy, alkylcarbonyloxyalkyl), amides (e.g. aminocarbonyl, mono- or di-alkylaminocarbonyl, aminocarbonylalkyl, mono- or di-alkylaminocarbonylalkyl, arylaminocarbonyl or arylalkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino or arylalkylcarbonylamino), carbamates (eg. alkoxycarbonylamino, aryloxycarbonylamino, arylalkyloxycarbonylamino, aminocarbonyloxy, mono- or di-alkylaminocarbonyloxy, arylaminocarbonyloxy or arylalkylaminocarbonyloxy) and ureas (eg. mono- or di-alkylaminocarbonylamino, arylaminocarbonylamino or arylalkylaminocarbonylamino);

nitrogen containing groups such as

amines (e.g. amino, mono- or dialkylamino, arylamino, aminoalkyl, mono- or dialkylaminoalkyl),

azides,

nitriles (e.g. cyano, cyanoalkyl),

nitro;

sulfur containing groups such as

thiols, thioethers, sulfoxides, and sulfones

(e.g. alkylthio, alkylsulfinyl, alkylsulfonyl, alkylthioalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, arylthio, arylsulfinyl, arylsulfonyl, arylthioalkyl, arylsulfinylalkyl, arylsulfonylalkyl)

and heterocyclic groups containing one or more, preferably one, heteroatom,

(e.g. thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, oxadiazolyl, thiadiazolyl, aziridinyl, azetidinyl, pyrrolidinyl, pyrrolinyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, tetrahydrofuranyl, pyranyl, pyronyl, pyridyl, pyrazinyl, pyridazinyl, piperidyl, hexahydroazepinyl, piperazinyl, morpholinyl, thianaphthyl, benzofuranyl, isobenzofuranyl, indolyl, oxyindolyl, isoindolyl, indazolyl, indolinyl, 7-azaindolyl, benzopyranyl, coumarinyl, isocoumarinyl, quinolinyl, isoquinolinyl, naphthridinyl, cinnolinyl, quinazolinyl, pyridopyridyl, benzoxazinyl, quinoxalinyl, chromenyl, chromanyl, isochromanyl, phthalazinyl and carbolinyl).

According to the second embodiment of the invention, alkyl and aryl groups may be substituted or unsubstituted. Where substituted, there will generally be 1 to 3 substituents present, preferably 1 substituent. According to the second embodiment of the invention, the substituent groups are selected from:

carbon containing groups such as

alkyl,

aryl,

arylalkyl (e.g. substituted and unsubstituted phenyl, substituted and unsubstituted benzyl);

halogen atoms and halogen containing groups such as

haloalkyl (e.g. trifluoromethyl);

oxygen containing groups such as

alcohols (e.g. hydroxy, hydroxyalkyl, aryl(hydroxy)alkyl),
ethers (e.g. alkoxy, alkoxyalkyl, aryloxyalkyl),
aldehydes (e.g. carboxaldehyde),
ketones (e.g. alkylcarbonyl, alkylcarbonylalkyl, arylcarbonyl, arylalkylcarbonyl, arylcarbonylalkyl)
acids (e.g. carboxy, carboxyalkyl),
acid derivatives such as esters (e.g. alkoxycarbonyl, alkoxycarbonylalkyl, alkylcarbonyloxy, alkylcarbonyloxyalkyl)
and amides (e.g. aminocarbonyl, mono- or dialkylaminocarbonyl, aminocarbonylalkyl, mono- or dialkylaminocarbonylalkyl, arylaminocarbonyl);

nitrogen containing groups such as
amines (e.g. amino, mono- or dialkylamino, aminoalkyl, mono- or dialkylaminoalkyl),
azides,
nitriles (e.g. cyano, cyanoalkyl),
nitro;

sulfur containing groups such as
thiols, thioethers, sulfoxides, and sulfones (e.g. alkylthio, alkylsulfinyl, alkylsulfonyl, alkylthioalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, arylthio, arylsulfinyl, arylsulfonyl, arylthioalkyl, arylsulfinylalkyl, arylsulfonylalkyl);

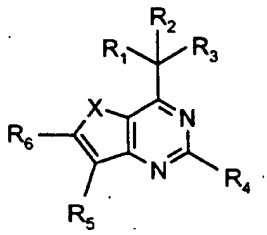
and heterocyclic groups containing one or more, preferably one, heteroatom (e.g. thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, pyrrolidinyl, pyrrolinyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, tetrahydrofuranyl, pyranyl, pyronyl, pyridyl, pyrazinyl, pyridazinyl, piperidyl, piperazinyl, morpholinyl, thianaphthyl, benzofuranyl, isobenzofuranyl, indolyl, oxyindolyl, isoindolyl,

indazolyl, indolinyl, 7-azaindolyl, benzopyranyl, coumarinyl, isocoumarinyl, quinolinyl, isoquinolinyl, naphthridinyl, cinnolinyl, quinazolinyl, pyridopyridyl, benzoxazinyl, quinoxalinyl, chromenyl, chromanyl, isochromanyl, phthalazinyl and carbolinyl).

According to the third embodiment of the invention, where any of R_1 to R_{12} is selected from alkyl and alkoxy, in accordance with formula (I) as defined above, then that alkyl group, or the alkyl group of the alkoxy group, may be substituted or unsubstituted. Where any of R_1 to R_{12} are selected from aryl and aryloxy, in accordance with formula (I) as defined above, then said aryl group, or the aryl group of the aryloxy group, may be substituted or unsubstituted. Where R_1 and R_2 together form a carbocyclic or heterocyclic ring, or R_5 and R_6 together form a carbocyclic or heterocyclic ring, in accordance with formula (I) as defined above, then that carbocyclic or heterocyclic ring may be substituted or unsubstituted. Where substituted, there will generally be 1 to 3 substituents present, preferably 1 substituent. In the third embodiment of the invention, the substituents are those defined in respect of the second embodiment of the invention described above.

According to the fourth embodiment of the invention, where any of R_1 to R_{12} is selected from alkyl and alkoxy, in accordance with formula (I) as defined above, then that alkyl group, or the alkyl group of the alkoxy group, may be substituted or unsubstituted. Where any of R_1 to R_{12} are selected from aryl and aryloxy, in accordance with formula (I) as defined above, then said aryl group, or the aryl group of the aryloxy group, may be substituted or unsubstituted. Where R_1 and R_2 together form a carbocyclic or heterocyclic ring, or R_5 and R_6 together form a carbocyclic or heterocyclic ring, in accordance with formula (I) as defined above, then that carbocyclic or heterocyclic ring may be substituted or unsubstituted. Where substituted, there will generally be 1 to 3 substituents present, preferably 1 substituent. In the fourth embodiment of the invention, the substituents may include those defined in respect of the first embodiment of the invention described above.

According to the fifth embodiment of the invention, the compounds are selected from compounds of formula (Ia):



(Ia)

wherein X, R_1 to R_3 and R_5 to R_{12} are as defined for formula (I) above;

R_4 is selected from hydrogen, alkyl, aryl, halogen, hydroxy, nitro, cyano, alkoxy, aryloxy, COR_7, $OCOR_7$, CO_2R_7, SR_7, SOR_7, SO_2R_7, $SO_2NR_7R_8$, $CONR_7R_8$, $CONR_7NR_8R_9$, $CONR_7YNR_8R_9$, $OCONR_7R_8$, NR_7R_8, NR_7YR_8, NR_7COR_8, $NR_7CONR_8R_9$, $NR_7ZCONR_8R_9$, $NR_7CO_2R_8$, $NR_7ZCO_2R_8$, $N(COR_8)COR_9$, $NR_7SO_2R_8$, $CR_7{=}NOR_8$, $NR_7CONR_8NR_9R_{10}$, $NR_7CONR_8YNR_9R_{10}$, $NR_7NR_8CO_2R_9$, $NR_7YNR_8CO_2R_9$, $NR_7NR_8CONR_9R_{10}$, $NR_7YNR_8CONR_9R_{10}$, $SO_2NR_7NR_8R_9$, $SO_2NR_7YNR_8R_9$, $NR_7SO_2NR_8R_9$, $NR_7NR_8SO_2R_9$, $NR_7YNR_8SO_2R_9$, $NR_7NR_8COR_9$, $NR_7YNR_8COR_9$, $NR_7NR_8R_9$, $NR_7YNR_8R_9$, $NR_7CSNR_8R_9$, $NR_7YNR_8CSNR_9R_{10}$ and $NR_7YNR_8CONR_9YNR_{10}R_{11}$;

Y is a divalent C_2 to C_4 carbon chain; and

Z is a divalent C_1 to C_4 carbon chain,

or a pharmaceutically acceptable salt thereof or prodrug thereof.

In the fifth embodiment of the invention, where any of R_1 to R_{12} is selected from alkyl and alkoxy, in accordance with formula (Ia) as defined above, then that alkyl group, or the alkyl group of the alkoxy group, may be substituted or unsubstituted. Where any of R_1 to R_{12} are selected from aryl and aryloxy, in accordance with formula (Ia) as defined above, then said aryl group, or the aryl group of the aryloxy group, may be substituted or unsubstituted. Where R_1 and R_2 together form a carbocyclic or heterocyclic ring, or R_5 and R_6 together form a carbocyclic or heterocyclic ring, in accordance with formula (Ia) as defined above, then that carbocyclic or heterocyclic ring may be substituted or unsubstituted. Where substituted, there will generally be 1 to 3 substituents present, preferably 1 substituent. In the fifth embodiment of the invention, the substituents may include those defined in respect of the first embodiment of the invention described above.

As used herein, the term "divalent C_1 to C_4 carbon chain" means a chain comprising 1, 2, 3 or 4 carbon atoms, branched or unbranched, and saturated or unsaturated.

As used herein, the term "divalent C_2 to C_4 carbon chain" means a chain comprising 2, 3 or 4 carbon atoms, branched or unbranched, and saturated or unsaturated.

In the compounds of the present invention, preferably X is S.

In a preferred embodiment of the invention, R_1 and R_2 are independently selected from hydrogen; hydroxy; cyano; alkyl, preferably hydroxy-substituted alkyl; and CO_2R_7, wherein preferably R_7 is alkyl. In this embodiment, it is preferred that R_1 and R_2 are selected from hydrogen and cyano. In this embodiment, it is preferred that one of R_1 and R_2 is hydrogen.

In a further embodiment, where R_1 is hydroxy, R_2 is not selected from hydroxy, alkoxy and aryloxy. Similarly, where R_2 is hydroxy, it is preferred that R_1 is not selected from hydroxy, alkoxy and aryloxy.

In an alternative further embodiment, where R_1 is selected from hydroxy and SH, R_2 is not selected from hydroxy, alkoxy, aryloxy and SR_7. Similarly, where R_2 is selected from hydroxy and SH, it is preferred that R_1 is not selected from hydroxy, alkoxy, aryloxy and SR_7.

In a preferred embodiment, R_1 and R_2 together form a carbonyl group or an oxime group, preferably a carbonyl group. Where R_1 and R_2 together form an oxime group $C = N - OR_{11}$, it is preferred that R_{11} is hydrogen.

In a particularly preferred embodiment of the invention, R_1 and R_2 together form a carbonyl group.

In the compounds of the present invention, it is preferred that R_3 is aryl, preferably comprising a five or six membered ring which may be substituted or unsubstituted and which may be carbocyclic or heterocyclic. It is preferred that R_3 is monocyclic.

Where R_3 is a five-membered ring, it is preferred that R_3 is an N, O or S-containing heterocyclic ring, preferably a thienyl, furyl, pyrrolyl or thiazolyl group, more preferably a thienyl group. Where R_3 is a six-membered ring it is preferred that R_3 is phenyl or an N-containing heterocyclic ring, preferably pyridyl.

Where R_3 is substituted, it is preferred that R_3 is substituted by substituent group(s) selected from halogen, preferably fluoro, chloro and bromo, more preferably chloro; lower alkyl, preferably methyl; lower alkoxy, preferably methoxy; nitro; and amino, preferably dialkylamino, more preferably dimethylamino.

In a particularly preferred embodiment, R_3 is selected from thienyl, furyl, pyridyl (preferably 2-pyridyl) and phenyl, preferably 2-thienyl. Where R_3 is selected from 2-thienyl, the 2-thienyl group is preferably unsubstituted or substituted by lower alkyl (preferably methyl) or halogen (preferably chloro or bromo, preferably chloro) or lower alkoxy (preferably methoxy), and more preferably is unsubstituted or substituted by lower alkyl (preferably methyl), and is more preferably unsubstituted. Where R_3 is selected from furyl, the furyl group is preferably a 2-furyl group and is preferably unsubstituted or substituted by lower alkyl (preferably methyl).

In the compounds of the present invention, preferably R_5 is selected from hydrogen, alkyl, halogen, hydroxy, nitro, cyano, alkoxy, aryloxy, COR_7, $OCOR_7$, CO_2R_7, SR_7, SOR_7, SO_2R_7, $SO_2NR_7R_8$, $CONR_7R_8$, $CONR_7NR_8R_9$, $OCONR_7R_8$, NR_7R_8, NR_7COR_8, $NR_7CONR_8R_9$, $NR_7CO_2R_8$, $NR_7SO_2R_8$, $CR_7{=}NOR_8$, $NR_7CONR_8NR_9R_{10}$, $NR_7NR_8CO_2R_9$, $NR_7NR_8CONR_9R_{10}$, $SO_2NR_7NR_8R_9$, $NR_7SO_2NR_8R_9$, $NR_7NR_8SO_2R_9$, $NR_7NR_8COR_9$, $NR_7NR_8R_9$, $NR_7CSNR_8R_9$, or together with R_6 forms a 5, 6 or 7 membered carbocyclic or heterocyclic ring.

In one embodiment of the present invention, R_5 is selected from hydrogen, halogen, alkyl and aryl.

Where R_5 is selected from aryl, it is preferred that R_5 is an aryl group other than phenyl or an N-containing heteroaromatic group, particularly pyridyl, pyrazinyl, pyrimidinyl and pyridazinyl. Where R_5 is an aryl group, it is preferred that R_5 is an aryl group selected from an

O- or S-containing heterocyclic ring, preferably an O-containing ring, and preferably a 5-membered heterocyclic ring, preferably furanyl or thienyl, and more preferably furanyl.

In the compounds of the present invention, preferably R_5 is selected from hydrogen, halogen and alkyl, and preferably R_5 is hydrogen.

In the compounds of the present invention, it is preferred that R_6 is selected from hydrogen, alkyl, aryl and halogen, and preferably R_6 is hydrogen.

It is preferred that at least one, and preferably both, of R_5 and R_6 are hydrogen. Where R_5 and/or R_6 are selected from alkyl, it is preferred that R_5 and/or R_6 are methyl.

Where any of R_1, R_2, or R_4 to R_6 are independently selected from $NR_7CO_2R_8$, it is preferred that R_8 is selected from alkyl and aryl.

Where any of R_1, R_2 or R_4 to R_6 are independently selected from $NR_7NR_8CO_2R_9$, it is preferred that R_9 is selected from alkyl and aryl.

Where R_4 is selected from $NR_7YNR_8CO_2R_9$, it is preferred that R_9 is selected from alkyl and aryl.

In the compounds of the present invention where R_4 is an NR_7R_8 group, the R_7 and R_8 groups may together form a ring to produce a cyclic amino group. The cyclic amino group is a saturated or partially unsaturated cyclic group (i.e. it is non-aromatic), and is preferably a saturated cyclic amino group. The cyclic amino group is preferably a 5-, 6- or 7-membered and is preferably a 5- or 6-membered cyclic amino group. Where partially unsaturated, it is preferred that only 1 double bond is present. The cyclic amino group may contain one or more additional heteroatoms, preferably one or two heteroatoms, wherein the heteroatoms are preferably selected from N, O and S and preferably from N and O. The cyclic amino groups may be substituted or unsubstituted, preferably substituted. Where substituted, there will generally be 1 to 3 substituents present, preferably 1 substituent. Substituents may include any of those set out above in respect of the first and second embodiments. Preferably the cyclic amino groups are selected from pyrrolidinyl, pyrrolidinonyl, piperidinyl, piperazinyl and

morpholinyl groups, more preferably from pyrrolidinyl, piperidinyl, piperazinyl and morpholinyl groups, and particularly from pyrrolidinyl groups (preferably substituted and preferably substituted by hydroxy, lower alkyl or hydroxy(lower alkyl)).

In one embodiment of the present invention, R_4 is preferably selected from alkyl (including trifluoromethyl); halogen (preferably chloro); alkoxy (preferably methoxy or ethoxy); SR_7 (preferably alkylthio, preferably methylthio); dialkylamino (preferably dimethylamino); and monoalkylamino, wherein said alkyl groups are substituted or unsubstituted. In this embodiment, preferably R_4 is unsubstituted alkyl, trifluoromethyl or monoalkylamino (wherein the alkyl groups are substituted or unsubstituted), and more preferably monoalkylamino (preferably NR_7R_8 wherein R_7 is hydrogen, and R_8 is substituted or unsubstituted). In this embodiment, where R_4 is monoalkylamino or dialkylamino, the alkyl group(s) may be substituted as described above, for instance, by hydroxy, alkoxy, amino or dialkylamino.

Where R_4 is alkyl, it is preferred that R_4 is unsubstituted alkyl (preferably saturated alkyl, preferably lower alkyl) or halo-substituted alkyl (preferably trifluoromethyl).

In a particularly preferred embodiment of the invention, R_4 is NR_7R_8. Where R_4 is NR_7R_8, it is preferred that R_7 is lower alkyl or hydrogen, and preferably hydrogen. Preferably, R_8 is lower alkyl (substituted or unsubstituted and, where substituted, is preferably substituted by hydroxy, alkoxy, a saturated heterocyclic group or aryl (particularly heteroaryl)), cyclic alkyl or aryl.

In a further preferred emdbodiment, R_4 is NH_2.

Where R_4 is $NR_7NR_8R_9$, it is preferred that R_7 is hydrogen. Preferably R_8 and R_9 are also hydrogen.

In the compounds of formula (I), preferably R_4 is selected from alkyl (including trifluoromethyl); halogen (preferably chloro); alkoxy (preferably methoxy or ethoxy; SR_7 (preferably methylthio); and a substituted amino group (preferably NR_7R_8, $NR_7NR_8COR_9$, $NR_7NR_8CO_2R_9$, $NR_7CO_2R_8$, $NR_7NR_8CONR_9R_{10}$, $NR_7NR_8SO_2R_9$, $NR_7NR_8CSNR_9R_{10}$, $NR_7NR_8R_9$ and NR_7COR_8, and more preferably NR_7R_8). Preferably R_4 is a substituted amino

group or alkyl. Most preferably R_4 is a substituted amino group, preferably NR_7R_8 wherein R_7 is hydrogen.

In the compounds of formula (Ia), preferably R_4 is selected from alkyl (including trifluoromethyl); halogen (preferably chloro); alkoxy (preferably methoxy or ethoxy; SR_7 (preferably methylthio); and a substituted amino group (preferably NR_7R_8, NR_7YR_8, $NR_7YNR_8COR_9$, $NR_7YNR_8CO_2R_9$, $NR_7ZCO_2R_8$, $NR_7YNR_8CONR_9R_{10}$, $NR_7YNR_8SO_2R_9$, $NR_7YNR_8CSNR_9R_{10}$, $NR_7NR_8R_9$ and $N(COR_8)COR_9$, and more preferably NR_7R_8). Preferably R_4 is a substituted amino group or alkyl. Most preferably R_4 is a substituted amino group, as detailed below.

In the compounds of formulae (I) or (Ia), in a preferred embodiment where R_4 is selected from NR_7R_8, it is preferred that R_7 is hydrogen or alkyl, and preferably hydrogen, and R_8 is selected from alkyl (preferably saturated alkyl), preferably lower alkyl (preferably saturated lower alkyl), substituted or unsubstituted and preferably substituted, wherein the preferred substituent groups on R_8 are selected from aryl (preferably thienyl, furyl, pyridyl and phenyl); oxygen-containing groups, particularly alcohols (preferably hydroxy), ethers (preferably alkoxy); acids (preferably carboxy); acid derivatives (particularly esters (preferably alkoxycarbonyl), amides (preferably alkylcarbonylamino and arylcarbonylamino), carbamates (preferably alkoxycarbonylamino and arylalkoxycarbonylamino) and ureas (preferably alkylaminocarbonylamino, arylaminocarbonylamino and arylalkylaminocarbonylamino); nitrogen-containing groups, particularly amines and thioureas; and saturated heterocyclic groups, particularly N- and O-containing groups (preferably tetrahydrofuranyl, pyrrolidinyl, pyrrolidinonyl, piperidinyl, piperazinyl and morpholinyl groups).

In the compounds of formulae (I) or (Ia), in an alternative preferred embodiment where R_4 is selected from NR_7R_8, it is preferred that R_7 is hydrogen or alkyl, and preferably hydrogen, and R_8 is selected from alkyl (preferably saturated alkyl), preferably lower alkyl (preferably saturated lower alkyl), substituted or unsubstituted and preferably substituted, wherein the preferred substituent groups on R_8 are selected from aryl (preferably phenyl); oxygen-containing groups, alcohols (preferably hydroxy), ethers (preferably alkoxy) and acid derivatives, particularly esters (preferably alkoxycarbonyl) and carbamates (preferably alkoxycarbonylamino); nitrogen-containing groups, particularly amines; and heterocyclic

groups, particularly saturated N-containing heterocyclic groups (preferably pyrrolidinyl, pyrrolidinonyl, piperidinyl, piperazinyl and morpholinyl groups).

In the compounds of formula (Ia) where R_4 is $NR_7YNR_8COR_9$, it is preferred that R_7 is hydrogen. Preferably R_8 is also hydrogen. Preferably R_9 is selected from lower alkyl, cyclic alkyl and aryl (preferably substituted or unsubstituted phenyl or thienyl).

In the compounds of formula (Ia) where R_4 is $NR_7YNR_8CO_2R_9$ or $NR_7YNR_8SO_2R_9$, it is preferred that R_7 is hydrogen. Preferably R_8 is also hydrogen. It is preferred that R_9 is selected from lower alkyl (substituted or unsubstituted and, where substituted, preferably substituted by halogen (preferably chloro) or aryl).

In the compounds of formula (Ia) where R_4 is $NR_7YNR_8CONR_9R_{10}$ or $NR_7YNR_8CSNR_9R_{10}$, it is preferred that R_7 is hydrogen. Preferably R_8 and R_9 are also hydrogen. It is preferred that R_{10} is lower alkyl (substituted or unsubstituted), cyclic alkyl or aryl.

In the compounds of formula (Ia) where R_4 is $NR_7ZCO_2R_8$, preferably R_7 is hydrogen and R_8 is selected from hydrogen and lower alkyl, and preferably from lower alkyl.

In the compounds of formula (Ia) where R_4 is NR_7YR_8, it is preferred that R_7 is hydrogen. R_8 is aryl, preferably substituted by lower alkyl, lower alkoxy and nitro.

In the compounds of formula (Ia) where R_4 is $N(COR_8)COR_9$, it is preferred that R_8 and R_9 are independently selected from lower alkyl.

In the compounds of formula (Ia), preferably Y is a saturated (alkylene) C_2 to C_4 carbon chain and is preferably unbranched . Preferably, Y is a C_2 or C_3 carbon chain, preferably a C_2 carbon chain. Preferably, Y is a divalent CH_2CH_2 radical.

In the compounds of formula (Ia), preferably Z is a saturated (alkylene) C_1 to C_4 carbon chain and is preferably unbranched . Preferably, Z is a C_1,C_2 or C_3 carbon chain, preferably a C_2 carbon chain. Preferably, Z is a divalent CH_2CH_2 radical.

In a particularly preferred embodiment of the invention, the compounds of the present invention are selected from:

(2R)-2-(1-Hydroxy-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

2-(3-(1H-Imidazol-1-yl)propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

(2RS)-2-(1-Hydroxy-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

2-(3-Hydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

3-Methyl-N-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)butanamide,

Methyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate,

2-(2-(1H-Imidazol-4-yl)ethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

(2RS)-2-(2,3-Dihydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

(2R)-2-(2-Hydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

2-(2-Hydroxyethylamino)thieno[3,2-d]pyrimidin-4-yl 3-methyl-2-thienylmethanone,

2-Chloroethyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate,

(2S)-2-(1-Hydroxy-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

2-(3-(1H-Imidazol-1-yl)propylamino)thieno[3,2-d]pyrimidin-4-yl 3-methyl-2-thienylmethanone,

N-(2-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)cyclohexyl-carboxamide,

Ethyl 4-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-ylamino)butanoate,

2-(2-Pyridylmethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

(2S)-2-(2-Hydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

N-Allyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea,

N-(2-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)acetamide,

2-(Tetrahydrofuran-2-ylmethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

N-Benzyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea,

2-(2-Hydroxyethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

Benzyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate, and

2-Aminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone.

In an alternative embodiment, the compounds of the present invention are selected from:

2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone,

2-(2-hydroxyethyl)aminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

2-ethylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

2-ethylthieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone,

2-methylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, and

2-(2-methoxyethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone.

Where chiral the compounds of the present invention may be in the form of a racemic mixture of pairs of enantiomers or in enantiomerically pure form.

According to a further aspect of the invention, there is provided for use in therapy a compound of the present invention, or a pharmaceutically acceptable salt or prodrug thereof.

The present invention may be employed in respect of a human or animal subject, more preferably a mammal, more preferably a human subject.

The disorders of particular interest are those in which the blocking of purine receptors, partiucularly adenosine receptors and more particularly adenosine A_{2A} receptors, may be beneficial. These may include movement disorders such as Parkinson's disease, drug-induced Parkinsonism, post-encephalitic Parkinsonism, Parkinsonism induced by poisoning (for example MPTP, manganese, carbon monoxide) and post-traumatic Parkinson's disease (punch-drunk syndrome).

Other movement disorders in which the blocking of purine receptors, may be of benefit include progressive supernuclear palsy, Huntingtons disease, multiple system atrophy, corticobasal degeneration, Wilsons disease, Hallerrorden-Spatz disease, progressive pallidal atrophy, Dopa-responsive dystonia-Parkinsonism, spasticity or other disorders of the basal ganglia which result in abnormal movement or posture. The present invention may also be effective in treating Parkinson's with on-off phenomena; Parkinson's with freezing (end of dose deterioration); and Parkinson's with prominent dyskinesias.

The compounds of the present invention may be used or administered in combination with one or more additional drugs useful in the treatment of movement disorders, such as L-

DOPA, the components being in the same formulation or in separate formulations for administration simultaneously or sequentially.

Other disorders in which the blocking of purine receptors, particularly adenosine receptors and more particularly adenosine A_{2A} receptors may be beneficial include acute and chronic pain; for example neuropathic pain, cancer pain, trigeminal neuralgia, migraine and other conditions associated with cephalic pain, primary and secondary hyperalgesia, inflammatory pain, nociceptive pain, tabes dorsalis, phantom limb pain, spinal cord injury pain, central pain, post-herpetic pain and HIV pain; affective disorders including mood disorders such as bipolar disorder, seasonal affective disorder, depression, manic depression, atypical depression and monodepressive disease; central and peripheral nervous system degenerative disorders including corticobasal degeneration, demyelinating disease (multiple sclerosis, disseminated sclerosis), Freidrich's ataxia, motoneurone disease (amyotrophic lateral sclerosis, progressive bulbar atrophy), multiple system atrophy, myelopathy, radiculopathy, peripheral neuropathy (diabetic neuropathy, tabes dorsalis, drug-induced neuropathy, vitamin deficiency), systemic lupus erythamatosis, granulomatous disease, olivo-ponto-cerebellar atrophy, progressive pallidal atrophy, progressive supranuclear palsy, spasticity; cognitive disorders including dementia, Alzheimers Disease, Frontotemporal dementia, multi-infarct dementia, AIDS dementia, dementia associated with Huntingtons Disease, Lewy body dementia, senile dementia, age-related memory impairment, cognitive impairment associated with dementia, Korsakoff syndrome, dementia pugilans; central nervous system injury including traumatic brain injury, neurosurgery (surgical trauma), neuroprotection for head injury, raised intracranial pressure, cerebral oedema, hydrocephalus, spinal cord injury; cerebral ischaemia including transient ischaemic attack, stroke (thrombotic stroke, ischaemic stroke, embolic stroke, haemorrhagic stroke, lacunar stroke) subarachnoid haemorrhage, cerebral vasospasm, neuroprotection for stroke, peri-natal asphyxia, drowning, cardiac arrest, subdural haematoma; myocardial ischaemia; muscle ischaemia; sleep disorders such as hypersomnia; eye disorders such as retinal ischaemia-reperfusion injury and diabetic neuropathy; cardiovascular disorders such as claudication; and diabetes and it's complications.

According to a further aspect of the present invention, there is provided the use of a compound of the present invention or a pharmaceutically acceptably salt or prodrug thereof in the

manufacture of a medicament for the treatment or prevention of a disorder in which the blocking of purine receptors, particularly adenosine receptors and more particularly A_{2A} receptors, may be beneficial.

According to a further aspect of the present invention there is provided a method of treating or preventing a disorder in which the blocking of purine receptors, particularly adenosine receptors and more particularly adenosine A_{2A} receptors, may be beneficial, the method comprising administration to a subject in need of such treatment an effective dose of a compound of the present invention or a pharmaceutically acceptable salt or prodrug thereof.

The disorder may be caused by the hyperfunctioning of the purine receptors.

According to a further aspect of the present invention there is provided use of a compound of the present invention or a pharmaceutically acceptable salt or prodrug thereof in the manufacture of a medicament for the treatment or prevention of movement disorders in a subject.

According to a further aspect of the invention there is provided a method of treating or preventing movement disorders comprising administration to a subject in need of such treatment an effective dose of a compound of the present invention or a pharmaceutically acceptable salt or prodrug thereof.

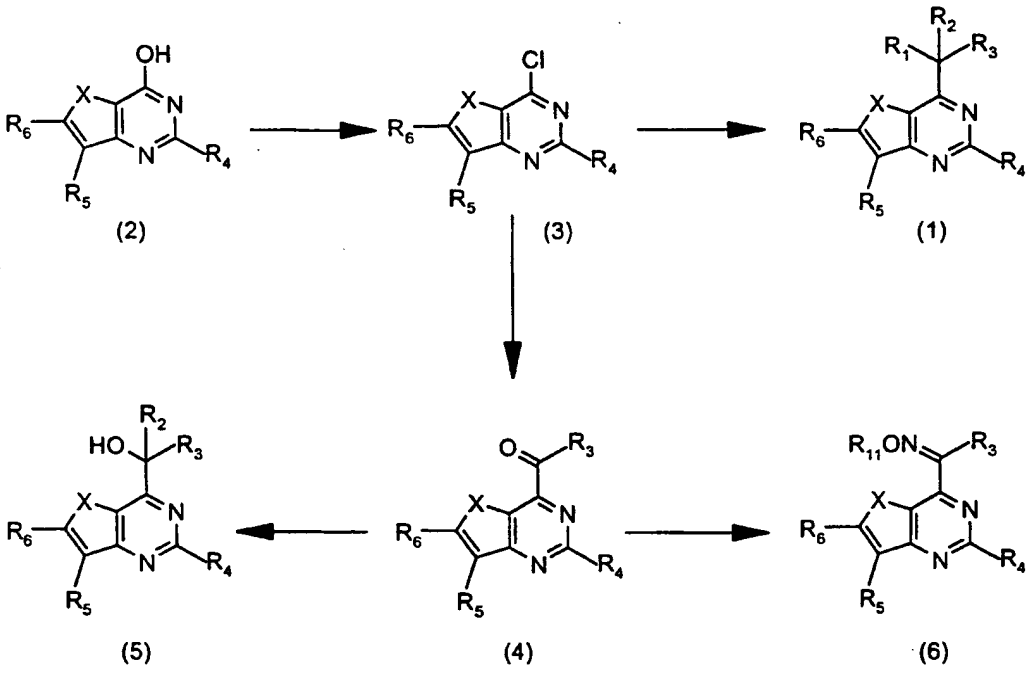
According to a further aspect of the invention there is provided use of a compound of the present invention or a pharmaceutically acceptable salt or prodrug thereof in the manufacture of a medicament for neuroprotection in a subject.

According to a further aspect of the invention there is provided a method of neuroprotection comprising administration to a subject in need of such treatment an effective dose of a compound of the present invention or a pharmaceutically acceptable salt or prodrug thereof.

The medicament for or method of neuroprotection may be of use in the treatment of subjects who are suffering from or at risk from a neurodegenerative disorder, such as a movement disorder.

According to a further aspect of the invention, there is provided a method of preparing the novel compounds of the present invention. Compounds of the present invention (according to formula (I) or formula (Ia)) may be prepared according to conventional synthetic methods, such as set out in Reaction Scheme 1.

Reaction Scheme 1



Alcohols (5) are prepared from ketones (4) either by reduction using standard methods such as $NaBH_4$ (where R_2 is H) or by addition of, for example, Grignard reagents (where R_2 is alkyl or aryl). Ketones (4) are prepared from chloro compounds (3) by known methods such as the addition of the appropriate aldehyde R_3CHO and a base such as NaH in the presence of a catalyst such as N,N-dimethylimidazolium iodide (Miyashita A. et al., *Heterocycles*, 1997, 45, 2159-2173). Chloro compounds (3) are either known or are prepared from alcohols (2) by standard methods such as treatment with $POCl_3$. Alcohols (2) are either known compounds or may be prepared by standard literature methods. Compounds of formula (3) where R_4 is a chloro group are either known or are prepared from compounds of formula (2) where R_4 is a hydroxy group by standard methods such as treatment with $POCl_3$. Compounds of formula (2) where R_4 is a hydroxy group are either known or are prepared by standard literature methods.

Oximes (6) are prepared from ketones (4) by standard methods such as treatment with the appropriate hydroxylamine in the presence of a base such as pyridine.

Compounds of formula (1) where R_1 is a nitrile, alkoxycarbonyl, nitro, sulphonyl or amide group are prepared from chloro compounds (3) by standard methods such as the addition of a compound of formula $HCR_1R_2R_3$, where R_1 is a nitrile, alkoxycarbonyl, nitro, sulphonyl or amide group, in the presence of a base such as NaH.

Compounds of formula (1) where R_1 is a hydroxymethyl group are prepared from compounds of formula (1) where R_1 is an alkoxycarbonyl group by standard methods such as reduction with, for example , DIBAL.

Compounds of formula (1) where R_4 is an alkoxy, aryloxy, hydroxy, alkylthio, arylthio, amino, mono or dialkylamino, cyano, carboxamido or substituted or unsubstituted hydrazino group may be prepared from compounds of formula (1) where R_4 is a halogen by standard methods such as reaction with the appropriate nucleophile. Appropriate nucleophiles would include for example alkoxides, aryloxides, hydroxide, alkylthiolates, arylthiolates, ammonia, mono or dialkylamines, cyanide, carboxamide salts, hydrazine and substituted hydrazines. Alternatively compounds of formula (1) where R_4 is an amino group may be prepared from compounds of formula (1) where R_4 is a halogen by standard methods such as reaction with an appropriately protected amino compound to form a compound of formula (1) where R_4 is a protected amine, followed by removal of the protecting group by standard methods. Appropriate protecting groups may include, for example, benzyl, dimethoxybenzyl, trialkylsilyl or trifluoroacetyl groups.

Compounds of formula (1) where R_4 is an acyloxy, carbamate, acylamino, semicarbazide, thiosemicarbazide, sulphonamide, urea, thiourea, sulphamide, acylhydrazine or sulphonylhydrazine group may be prepared by derivatisation of the corresponding compound of formula (1) where R_4 is a hydroxy, mercapto, amino, monoalkylamino or hydrazino group using standard literature methods.

Compounds of formula (1) where R_4 is a sulphonyl or sulphinyl group may be prepared from compounds of formula (1) where R_4 is an alkylthio or arylthio group by standard methods such as oxidation with an appropriate reagent.

Compounds of formula (1) where R_4 is a group containing an amino substituent, for example an aminoalkyl group or an aminoalkylamino group such as an ethylenediamine group, may be further derivatised using standard methods as described above. For example the amino group may be converted into an alkylamine, amide, carbamate, urea, thiourea, sulphonamide or sulphamide by using standard literature methods such as alkylation, reductive alkylation, acylation, sulphonylation or reaction with an appropriate isocyanate.

Compounds of formula (1) where R_4 is an ester, amide or hydrazide may be prepared from compounds of formula (1) where R_4 is a halogen by standard methods such as carbonylation reactions. Alternatively compounds of formula (I) where R_4 is an ester group may be prepared from compounds of formula (2) where R_4 is an ester group by the methods described above. Compounds of formula (2) where R_4 is an ester group are known in the literature. Further modification of a compound of formula (1) where R_4 is an ester or amide can lead, by using standard literature methods, to compounds of formula (1) where R_4 is for example an aldehyde, carboxylic acid, oxime, amidine, hydroxyalkyl, or aminoalkyl group. Further modification of a compound of formula (1) where R_4 is an ester, amide, hydrazide, amidine, aldehyde or carboxylic acid can lead, by the use of standard literature methods, to compounds of formula (1) where R_4 is, for example a 5- or 6-membered heterocyclic group such as oxadiazole, thiadiazole, thiazole, oxazole, isoxazole, pyrazole, triazole, imidazole or pyrimidine.

Compounds of formula (1) where R_1 is an alkoxy, acyloxy or carbamate group may be prepared from compounds of formula (1) where R_1 is a hydroxy group by standard methods such as alkylation, acylation or by reaction with an appropriate isocyanate.

Compounds of formula (1) where R_1 is an amino, alkylamino, acylamino, sulphonylamino, urea or sulphamide may be prepared from compounds of formula (1) where R_1 is an amino group by standard methods such as alkylation, acylation, sulphonylation or by reaction with an appropriate isocyanate.

Compounds of formula (1) where R_1 is an amino group may be prepared from a compound of formula (1) where R_1 is a nitro group by standard methods such as reduction. Alternatively compounds of formula (1) where R_1 is an amino group may be prepared from a compound of formula (1) where R_1 and R_2 together form a carbonyl group by standard methods such a reductive amination.

Compounds of formula (1) where R_1 is a hydrazino group may be prepared from compounds of formula (1) where R_1 is a hydroxy group by standard methods such as conversion of the hydroxy group into a suitable leaving group, for example a mesylate or tosylate group, followed by displacement with hydrazine or an appropriately substituted hydrazine. Further derivatisation of the hydrazine group, if required, may be achieved by standard methods such as for example acylation or sulphonylation.

Compounds of formula (1) where R_1 and R_2 together form an imine group ($C=N-R_{11}$) or a hydrazone group ($C=NNR_{11}R_{12}$) may be prepared from compounds of formula (4) by standard methods such as treatment with the appropriate amine or hydrazine.

Compounds of formula (1) where R_5 is an aryl (including heteroaryl) group may be prepared from compounds of formula (1) where R_5 is a halogen by standard methods such as a palladium catalysed aryl coupling reaction such as a Suzuki coupling or a Stille coupling reaction. Compounds of formula (1) where R_5 is a halogen are prepared from compounds of formula (3) where R_5 is a halogen according to Reaction Scheme 1. Compounds of formula (3) where R_5 is a halogen are known in the literature.

Compounds of formula (1) where R_5 is an amino group may be prepared from compounds of formula (1) where R_5 is a nitro group by standard methods such as reduction. Further modification of compounds of formula (1) where R_5 is an amino group can lead, by the use of standard methods, to compounds of formula (1) where R_5 is an alkylamino, acylamino, carbamate, urea, thiourea, sulphonamide or sulphamide group as described above. Compounds of formula (1) where R_5 is a nitro group may be prepared from compounds of formula (3) where R_5 is a nitro group according to Reaction Scheme 1. Compounds of formula (3) where R_5 is a nitro group are known in the literature.

According to a further aspect of the invention, there is provided a pharmaceutical composition comprising a compound of the present invention in combination with a pharmaceutically acceptable carrier or excipient and a method of making such a composition comprising combining a compound of the present invention with a pharmaceutically acceptable carrier or excipient.

The pharmaceutical compositions employed in the present invention comprise a compound of the present invention, or pharmaceutically acceptable salts or prodrugs thereof, and may also contain a pharmaceutically acceptable carrier and optionally other therapeutic ingredients known to those skilled in the art. The term, "pharmaceutically acceptable salts", refers to salts prepared from pharmaceutically acceptable non-toxic acids including inorganic acids and organic acids.

Where the compounds of the present invention are basic, salts may be prepared from pharmaceutically acceptable non-toxic acids including inorganic and organic acids. Such acids include acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethenesulfonic, fumaric, gluconic, glutamic, hippuric, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, oxalic, p-toluenesulfonic and the like. Particularly preferred are hydrochloric, hydrobromic, phosphoric, and sulfuric acids, and most particularly preferred is the hydrochloride salt.

Any suitable route of administration may be employed for providing the patient with an effective dosage of a compound of the present invention. For example, oral, rectal, parenteral (intravenous, intramuscular), transdermal, subcutaneous, and the like may be employed. Dosage forms include tablets, troches, dispersions, suspensions, solutions, capsules, patches, and the like. The most suitable route in any given case will depend on the severity of the condition being treated. The most preferred route of administration of the present invention is the oral route. The compositions may be conveniently presented in unit dosage form and prepared by any of the methods well known in the art of pharmacy.

In practical use, the compounds of the present invention can be combined as the active ingredient in intimate admixture with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques. The carrier may take a wide variety of forms depending on the form of preparation desired for administration, *e.g.* oral or parenteral (*e.g.* intravenous). In preparing the compositions for oral dosage form, any of the usual pharmaceutical media may be employed as carriers, such as, for example, water, glycols, oils, alcohols, flavouring agents, preservatives, colouring agents, and the like in the case of oral liquid preparations (such as suspensions, solutions and elixirs) or aerosols; or carriers such as starches, sugars, micro-crystalline cellulose, diluents, granulating agents, lubricants, binders, disintegrating agents, and the like may be used in the case of oral solid preparations such as, for example, powders, capsules, and tablets, with the solid oral preparations being preferred over the liquid preparations. The most preferred solid oral preparation is tablets.

Because of their ease of administration, tablets and capsules represent the most advantageous oral dosage unit form in which case solid pharmaceutical carriers are employed. If desired, tablets may be coated by standard aqueous or non-aqueous techniques.

In addition to the common dosage forms set out above, the compounds of the present invention may also be administered by controlled release means and/or delivery devices such as those described in United States Patent Nos.: 3,845,770; 3,916,899; 3,536,809; 3,598,123; 3,630,200; 4,008,719; 4,687,660; and 4,769,027, the disclosures of which are hereby incorporated by reference.

Pharmaceutical compositions employed in the present invention suitable for oral administration may be presented as discrete units such as capsules, cachets, or tablets, or aerosol sprays each containing a predetermined amount of the active ingredient as a powder or granules, a solution or a suspension in an aqueous liquid, an oil-in-water emulsion, or a water-in-oil liquid emulsion. Such compositions may be prepared by any of the methods of pharmacy, but all methods include the step of bringing the active ingredient into association with the carrier which constitutes one or more necessary ingredients. In general, the compositions are prepared by uniformly and intimately admixing the active ingredient with

liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product into the desired presentation.

For example, a tablet may be prepared by compression or moulding, optionally with one or more accessory ingredients. Compressed tablets may be prepared by compressing in a suitable machine the active ingredient in a free-flowing form such as powder or granules, optionally mixed with a binder, a lubricant, an inert diluent, and/or a surface active or dispersing agent. Moulded tablets may be made by moulding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent.

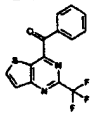
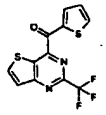
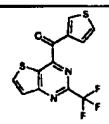
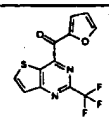
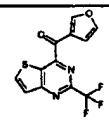
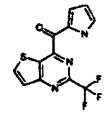
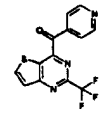
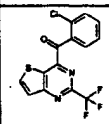
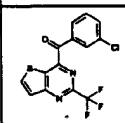
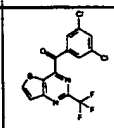
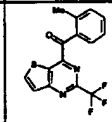
The invention is further defined by reference to the following examples. It will be apparent to those skilled in the art that many modifications, both to materials and methods, may be practised without departing from the purpose and interest of this invention.

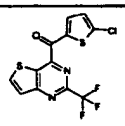
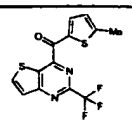
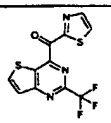
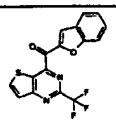
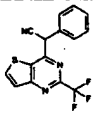
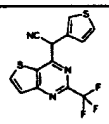
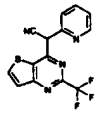
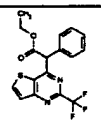
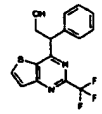
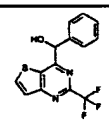
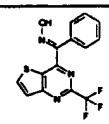
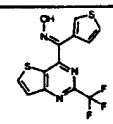
EXAMPLES

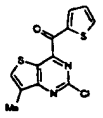
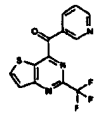
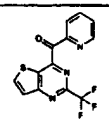
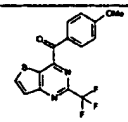
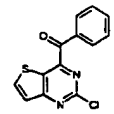
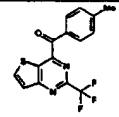
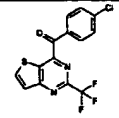
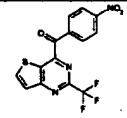
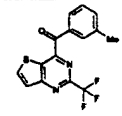
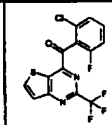
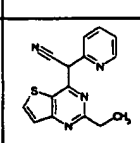
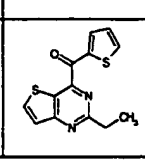
Synthetic Examples

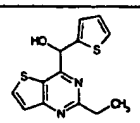
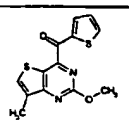
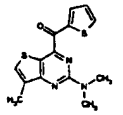
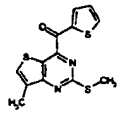
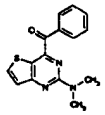
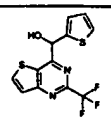
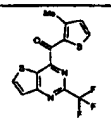
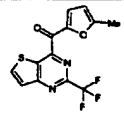
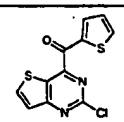
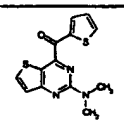
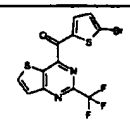
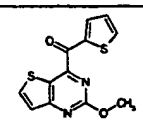
The invention is illustrated with reference to Examples 1 to 170, as set out in Table 1. The syntheses of Examples 1 to 170 is described in Table 2 with reference to the general Synthetic Methods set out hereinafter. The analytical data for Examples 1 to 170 is given in Table 2.

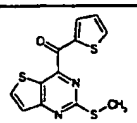
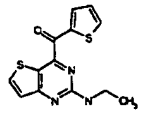
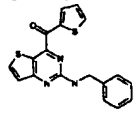
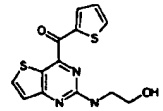
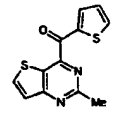
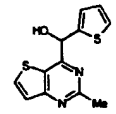
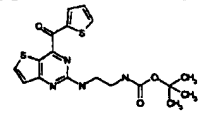
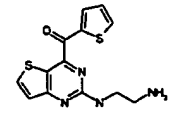
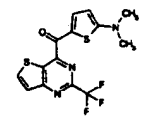
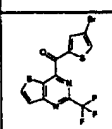
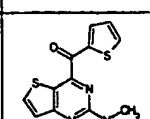
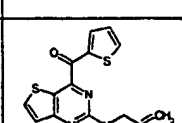
Table 1

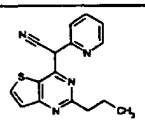
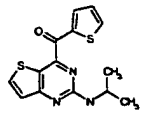
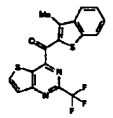
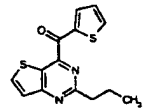
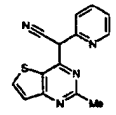
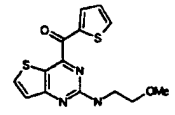
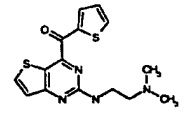
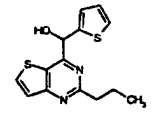
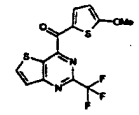
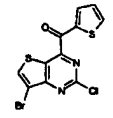
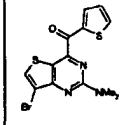
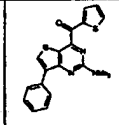
Example	Structure	Compound Name
1		Phenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
2		2-Thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
3		3-Thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
4		2-Furyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
5		3-Furyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
6		2-Pyrrolyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
7		4-Pyridyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
8		2-Chlorophenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
9		3-Chlorophenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
10		3,5-Dichlorophenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
11		2-Methylphenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone

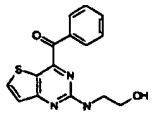
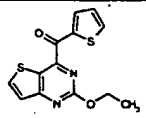
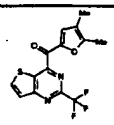
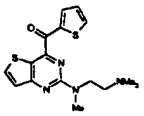
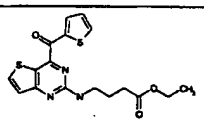
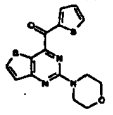
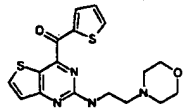
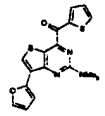
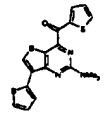
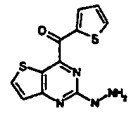
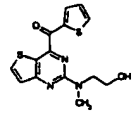
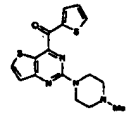
12		5-Chloro-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
13		5-Methyl-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
14		2-Thiazolyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
15		2-Benzofuranyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
16		α-Phenyl-2-trifluoromethylthieno[3,2-d]pyrimidine-4-acetonitrile
17		α-(3-Thienyl)-2-trifluoromethylthieno[3,2-d]pyrimidine-4-acetonitrile
18		α-(2-Pyridyl)-2-trifluoromethylthieno[3,2-d]pyrimidine-4-acetonitrile
19		Ethyl α-phenyl-2-trifluoromethylthieno[3,2-d]pyrimidine-4-acetate
20		β-Phenyl-2-trifluoromethylthieno[3,2-d]pyrimidine-4-ethanol
21		α-Phenyl-2-trifluoromethylthieno[3,2-d]pyrimidine-4-methanol
22		Phenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone oxime
23		3-Thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone oxime

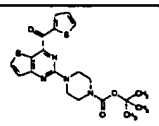
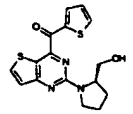
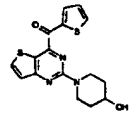
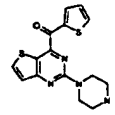
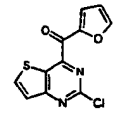
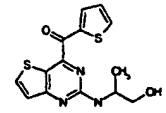
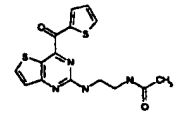
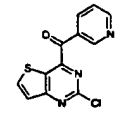
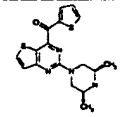
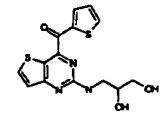
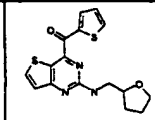
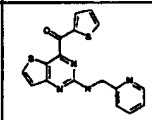
24		2-Chloro-7-methylthieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
25		3-Pyridyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
26		2-Pyridyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
27		4-Methoxyphenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
28		2-Chlorothieno[3,2-d]pyrimidin-4-yl phenylmethanone
29		4-Methylphenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
30		4-Chlorophenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
31		4-Nitrophenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
32		3-Methylphenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
33		2-Chloro-6-fluorophenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
34		2-Ethyl-α-(2-pyridyl)thieno[3,2-d]pyrimidine-4-acetonitrile
35		2-Ethylthieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone

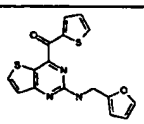
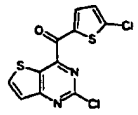
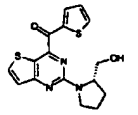
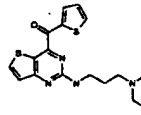
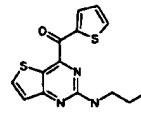
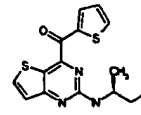
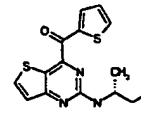
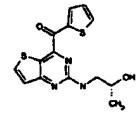
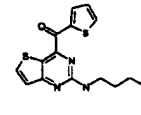
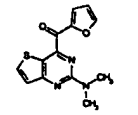
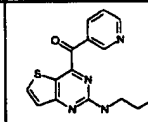
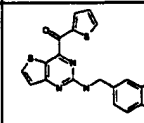
36		2-Ethyl-α-(2-thienyl)thieno[3,2-d]pyrimidine-4-methanol
37		2-Methoxy-7-methylthieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
38		2-Dimethylamino-7-methylthieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
39		7-Methyl-2-methylthiothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
40		2-Dimethylaminothieno[3,2-d]pyrimidin-4-yl phenylmethanone
41		α-(2-Thienyl)-2-trifluoromethylthieno[3,2-d]pyrimidine-4-methanol
42		3-Methyl-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
43		5-Methyl-2-furyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
44		2-Chlorothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
45		2-Dimethylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
46		5-Bromo-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
47		2-Methoxythieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone

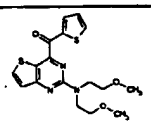
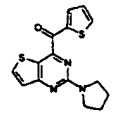
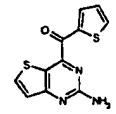
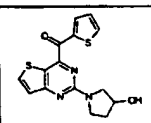
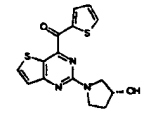
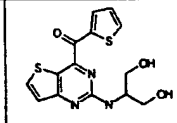
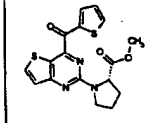
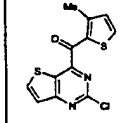
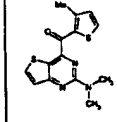
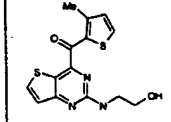
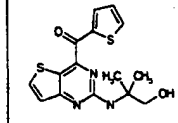
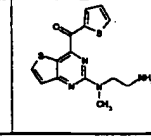
48		2-Methylthiothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
49		2-Ethylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
50		2-Benzylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
51		2-(2-Hydroxyethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
52		2-Methylthieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
53		2-Methyl-α-(2-thienyl)thieno[3,2-d]pyrimidine-4-methanol
54		Tert-butyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate
55		2-(2-Aminoethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone dihydrochloride
56		5-Dimethylamino-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
57		4-Bromo-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
58		2-Methylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
59		2-Allylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone

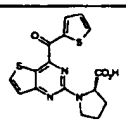
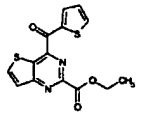
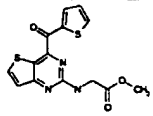
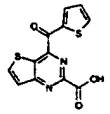
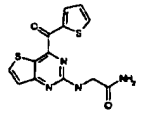
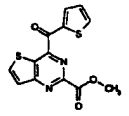
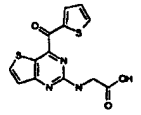
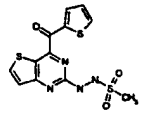
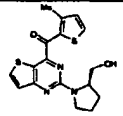
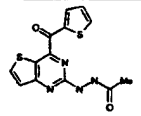
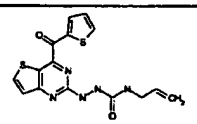
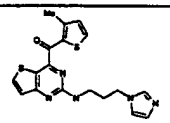
60		2-*n*-Propyl-α-(2-pyridyl)thieno[3,2-d]pyrimidine-4-acetonitrile
61		2-Isopropylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
62		3-Methylbenzothiophene-2-yl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
63		2-*n*-Propylthieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
64		2-Methyl-α-(2-pyridyl)thieno[3,2-d]pyrimidine-4-acetonitrile
65		2-(2-Methoxyethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
66		2-(2-Dimethylaminoethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone dihydrochloride
67		2-*n*-Propyl-α-(2-thienyl)thieno[3,2-d]pyrimidine-4-methanol
68		5-Methoxy-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
69		7-Bromo-2-chlorothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
70		7-Bromo-2-dimethylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
71		2-Dimethylamino-7-phenylthieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone

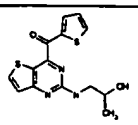
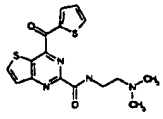
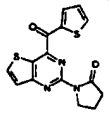
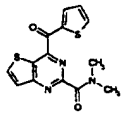
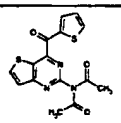
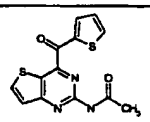
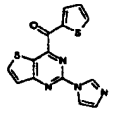
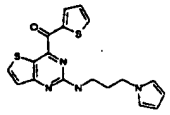
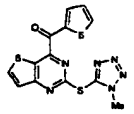
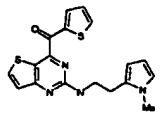
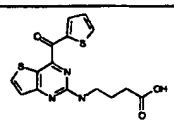
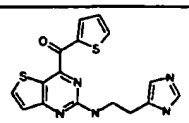
72		2-(2-Hydroxyethylamino)thieno[3,2-d]pyrimidin-4-yl phenylmethanone
73		2-Ethoxythieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
74		4,5-Dimethyl-2-furyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone
75		2-(N-(2-Dimethylaminoethyl)-N-methylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone dihydrochloride
76		Ethyl 4-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-ylamino)butanoate
77		2-(4-Morpholinyl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
78		2-(2-(4-Morpholinyl)ethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
79		2-Dimethylamino-7-(2-furyl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
80		2-Dimethylamino-7-(2-thienyl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
81		2-Hydrazinothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
82		2-(N-(2-Hydroxyethyl)-N-methylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
83		2-(4-Methylpiperazinyl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone

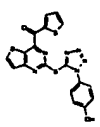
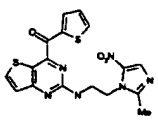
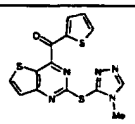
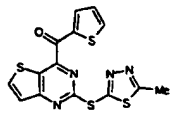
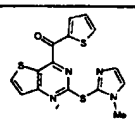
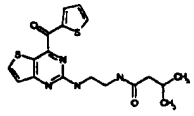
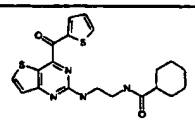
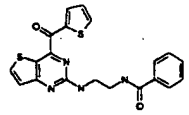
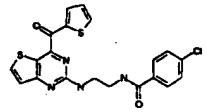
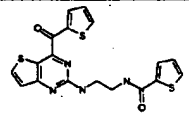
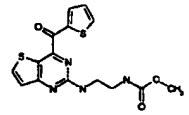
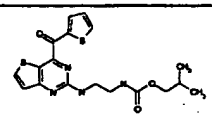
84		Tert-butyl 4-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)piperazinecarboxylate
85		(2R)-2-(2-Hydroxymethylpyrrolidin-1-yl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
86		2-(4-Hydroxypiperidin-1-yl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
87		2-(1-Piperazinyl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
88		2-Chlorothieno[3,2-d]pyrimidin-4-yl 2-furylmethanone
89		(2RS)-2-(1-Hydroxy-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
90		N-(2-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)acetamide
91		2-Chlorothieno[3,2-d]pyrimidin-4-yl 3-pyridylmethanone
92		Cis-2-(3,5-dimethyl-1-piperazinyl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
93		(2RS)-2-(2,3-Dihydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
94		2-(Tetrahydrofuran-2-ylmethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
95		2-(2-Pyridylmethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone

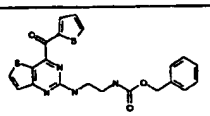
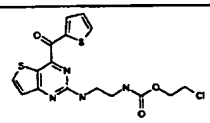
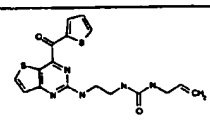
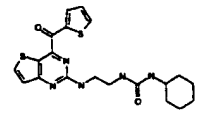
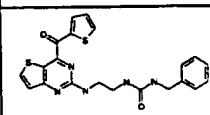
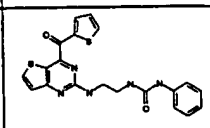
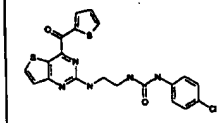
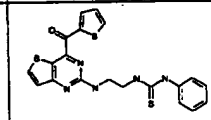
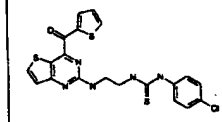
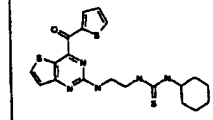
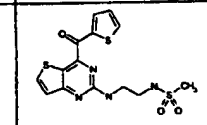
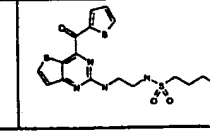
96		2-(2-Furylmethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
97		2-Chlorothieno[3,2-d]pyrimidin-4-yl 5-chloro-2-thienylmethanone
98		(2S)-2-(2-Hydroxymethylpyrrolidin-1-yl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
99		2-(3-(Morpholin-4-yl)propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
100		2-(3-Hydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
101		(2S)-2-(1-Hydroxy-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
102		(2R)-2-(1-Hydroxy-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
103		(2R)-2-(2-Hydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
104		2-(3-(1H-Imidazol-1-yl)propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
105		2-Dimethylaminothieno[3,2-d]pyrimidin-4-yl 2-furylmethanone
106		2-(2-Hydroxyethylamino)thieno[3,2-d]pyrimidin-4-yl 3-pyridylmethanone
107		2-(3,4-Dimethoxybenzylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone

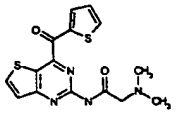
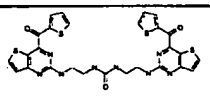
108		2-(N,N-Bis(2-methoxyethyl)amino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
109		2-(Pyrrolidin-1-yl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
110		2-Aminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
112		(3RS)-2-(3-Hydroxypyrrolidin-1-yl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
113		(3R)-2-(3-Hydroxypyrrolidin-1-yl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
114		2-(1,3-Dihydroxy-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
115		(2S)-N-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)proline methyl ester
116		2-Chlorothieno[3,2-d]pyrimidin-4-yl 3-methyl-2-thienylmethanone
117		2-Dimethylaminothieno[3,2-d]pyrimidin-4-yl 3-methyl-2-thienylmethanone
118		2-(2-Hydroxyethylamino)thieno[3,2-d]pyrimidin-4-yl 3-methyl-2-thienylmethanone
119		2-(1-Hydroxy-2-methyl-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
120		2-(N-(2-Aminoethyl)-N-methylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone

121		(2R)-N-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)proline
122		Ethyl 4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-carboxylate
123		Methyl (4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-ylamino)acetate
124		4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-carboxylic acid
125		(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-ylamino)acetamide
126		Methyl 4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-carboxylate
127		(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-ylamino)acetic acid
128		Methanesulphonic acid 2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)hydrazide
129		(2R)-2-(2-Hydroxymethylpyrrolidin-1-yl)thieno[3,2-d]pyrimidin-4-yl 3-methyl-2-thienylmethanone
130		Acetic acid 2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)hydrazide
131		N-Allyl-2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)hydrazinecarboxamide
132		2-(3-(1H-Imidazol-1-yl)propylamino)thieno[3,2-d]pyrimidin-4-yl 3-methyl-2-thienylmethanone

133		(2S)-2-(2-Hydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
134		N-(2-Dimethylaminoethyl)-4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-carboxamide
135		1-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)-2-pyrrolidinone
136		N,N-Dimethyl-4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-carboxamide
137		N-Acetyl-N-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)acetamide
138		N-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)acetamide
139		2-(1H-Imidazol-1-yl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
140		2-(3-(1H-Pyrrol-1-yl)propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
141		2-(1-Methyl-1H-tetrazol-5-ylthio)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
142		2-(2-(1-Methyl-1H-pyrrol-2-yl)ethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
143		4-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-ylamino)butanoic acid
144		2-(2-(1H-Imidazol-4-yl)ethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone

145		2-(1-(4-Hydroxyphenyl)-1H-tetrazol-5-ylthio)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
146		2-(2-(2-Methyl-5-nitro-1H-imidazol-1-yl)ethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
147		2-(4-Methyl-4H-[1,3,4]triazol-3-ylthio)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
148		2-(5-Methyl-[1,3,4]-thiadiazol-2-ylthio)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
149		2-(1-Methyl-1H-imidazol-2-ylthio)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone
150		3-Methyl-N-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)butanamide
151		N-(2-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)cyclohexylcarboxamide
152		N-(2-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)benzamide
153		4-Chloro-N-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)benzamide
154		N-(2-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)-2-thiophenecarboxamide
155		Methyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate
156		2-Methylpropyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate

157		Benzyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate
158		2-Chloroethyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate
159		N-Allyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea
160		N-Cyclohexyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea
161		N-Benzyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea
162		N-Phenyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea
163		N-(4-Chlorophenyl)-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea
164		N-Phenyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)thiourea
165		N-(4-Chlorophenyl)-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)thiourea
166		N-Cyclohexyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)thiourea
167		N-(2-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)methanesulphonamide
168		N-(2-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)butanesulphonamide

169		2-Dimethylamino-N-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)acetamide hydrochloride
170		N,N'-Bis(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea

Synthetic Methods

Method A

Phenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone (Example 1)

A suspension of 4-chloro-2-trifluoromethylthieno[3,2-d]pyrimidine (0.3 g, 1.26 mmol), benzaldehyde (0.28 g, 2.64 mmol) and N,N-dimethylimidazolium iodide (0.2 g, 0.89 mmol) in THF (8 mL) was treated with NaH (60 % dispersion in oil, 0.112 g, 2.8 mmol), refluxed for 15 min, cooled to room temperature, treated with water (4 mL) and the organic phase separated. The aqueous phase was extracted with CH_2Cl_2 (2 x 20 mL), the combined organic phase washed with brine (10 mL), dried ($MgSO_4$), concentrated *in vacuo* and the resulting brown oil purified by chromatography [SiO_2; heptane-EtOAc (3:1)] then recrystallised from heptane to give the *title compound* (280 mg, 43 %) as yellow needles.

Method B

α-Phenyl-2-trifluoromethylthieno[3,2-d]pyrimidine-4-acetonitrile (Example 16)

A suspension of NaH (60 % dispersion in oil, 60 mg, 1.5 mmol) in DMF (5 mL) and toluene (15 mL) at room temperature was treated with phenylacetonitrile (0.16 g, 1.37 mmol), stirred for 10 min, treated with a solution of 4-chloro-2-trifluoromethylthieno[3,2-d]pyrimidine (0.3 g, 1.26 mmol) in DMF (2 mL), stirred for 15 min, treated with water (5 mL) and the phases separated. The aqueous phase was extracted with EtOAc (2 x 50 mL), the combined organic phase washed with water (3 x 10 mL), brine (10 mL), dried ($MgSO_4$), concentrated *in vacuo* and the resulting orange oily solid crystallised from heptane to give the *title compound* (0.1 g, 25 %) as a gold solid.

Method C

β-Phenyl-2-trifluoromethylthieno[3,2-d]pyrimidine-4-ethanol (Example 20)

A solution of ethyl α-phenyl-2-trifluoromethylthieno[3,2-d]pyrimidine-4-acetate (0.21 g, 0.57 mmol) in Et_2O (5 mL) at –78 °C was treated dropwise with 1-M DIBAL in toluene (1.6 mL, 1.6 mmol), stirred at –78 °C for 15 min, warmed to room temperature, treated with water (2 mL) and extracted with Et_2O (5 mL). The extract was washed with brine (10 mL), dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography [SiO_2; heptane-EtOAc (3:1)] to give the *title compound* (67 mg, 36 %) as a brown oil.

Method D

2-Ethyl-α-(2-thienyl)thieno[3,2-d]pyrimidine-4-methanol (Example 36)

A solution of 2-ethylthieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (170 mg, 0.6 mmol) in MeOH (10 mL) at room temperature was treated with $NaBH_4$ (26 mg, 0.7 mmol), stirred for 1.5 h, concentrated *in vacuo*, treated with water (10 mL), extracted with EtOAc (2 x 10 mL) and purified by chromatography [SiO_2; EtOAc] to give the *title compound* (109 mg, 64 %) as a pale yellow solid.

Method E

Phenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone oxime (Example 22)

A solution of phenyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone (60 mg, 0.19 mmol) and hydroxylamine hydrochloride (0.04 g, 0.58 mmol) in pyridine (2 mL) was refluxed for 1 h, concentrated *in vacuo*, treated with toluene (2 mL), concentrated *in vacuo* and the resulting solid dissolved in EtOAc (5 mL), washed with water (3 mL) and concentrated *in vacuo* to give the *title compound* (62 mg, 98 %), a mixture of geometrical isomers, as an oily solid.

Method F

2-Ethylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (Example 49)

A suspension of 2-chlorothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (0.196 g, 0.7 mmol) in EtOH (5 mL) was treated with 12.4-M ethylamine in water (0.06 mL, 0.7 mmol), refluxed for 16 h, cooled, treated with water (5 mL) and the resulting solid filtered and recrystallised [EtOAc – heptane] to give the *title compound* (0.138 g, 68 %) as a yellow solid.

Method G

2-(2-Aminoethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone dihydrochloride (Example 55)

A solution of 2-(2-butoxycarbonylaminoethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (58 mg, 0.14 mmol) in MeOH (5 mL) was treated with 4-M HCl in dioxane (0.5 mL), stirred at room temperature for 16 h and the resulting solid filtered and washed with ether to give the *title compound* (41 mg, 77 %) as a white crystalline solid.

Method H

5-Dimethylamino-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone (Example 56)

A suspension of 5-bromo-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone (0.3 g, 0.76 mmol) in EtOH (20 mL) was treated with 40 % aqueous dimethylamine (5 mL), refluxed for 1 h, cooled, treated with water (25 mL), concentrated *in vacuo* and the aqueous mixture extracted with EtOAc (2 x 25 mL), the combined extracts washed with brine (25 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The resulting red oil was purified by chromatography [SiO_2; heptane – EtOAc (1:1)] to give the *title compound* (0.115 g, 42 %) as a red solid.

Method I

5-Methoxy-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone (Example 68)

A suspension of 5-bromo-2-thienyl 2-trifluoromethylthieno[3,2-d]pyrimidin-4-ylmethanone (0.2 g, 0.51 mmol) in MeOH (15 mL) was treated with sodium methoxide (0.11 g, 2.04 mmol), refluxed for 1 h, treated with dioxane (0.1 mL) to aid dissolution, refluxed for 18 h, cooled, treated with water (15 mL) and concentrated *in vacuo*. The resulting aqueous mixture was extracted with EtOAc (2 x 25 mL), the combined extracts washed with brine (25 mL), dried ($MgSO_4$), concentrated *in vacuo* and the resulting red oil dissolved in heptane – EtOAc (50:50), filtered through a pad of SiO_2, concentrated *in vacuo* and the resulting solid recrystallised [heptane – EtOAc (19:1)] to give the *title compound* (0.124 g, 71 %) as a yellow solid.

Method J

2-Dimethylamino-7-phenylthieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (Example 71)

A solution of palladium(II) acetate (2.1 mg, 9.5 μmol) and triphenylphosphine (10.0 mg, 38 μmol) in DMF (1 mL) was stirred under an atmosphere of argon at room temperature for 5 min, treated with a solution of 7-bromo-2-dimethylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (0.07 g, 0.2 mmol) in DMF (4 mL), stirred for a further 5 min, treated with phenylboronic acid (0.46 g, 0.4 mmol) in EtOH (0.7 mL) followed by saturated $NaHCO_3$ (0.7 mL) and stirred at 80 °C for 2 h. The reaction mixture was cooled to room temperature, extracted with Et_2O (2 x 5 mL), the combined organic phase washed with water (5 mL), dried ($MgSO_4$), concentrated *in vacuo* and the resulting residue purified by chromatography [SiO_2; heptane-EtOAc (95:5)] to give the *title compound* (61 mg, 87 %) as an orange solid.

Method K

2-Dimethylamino-7-(2-furyl)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (Example 79)

A mixture of palladium(II) acetate (4.1 mg, 18.3 μmol) and triphenylarsine (22.4 mg, 73 μmol) in DMF (0.8 mL) was stirred under an atmosphere of argon at room temperature for 10 min, treated with a solution of 7-bromo-2-dimethylaminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (0.067 g, 0.18 mmol) in DMF (1.1 mL), stirred for 10 min then treated dropwise with 2-tri-*n*-butylstannylfuran (104 μL, 0.33 mmol). The reaction mixture was stirred at 100 °C for 117 h, cooled, poured into saturated NH_4Cl (5 mL), extracted with EtOAc (4 x 5 mL), the combined organic phase washed with water (5 mL), dried ($MgSO_4$), concentrated *in vacuo* and the resulting residue purified by chromatography [SiO_2; heptane-EtOAc (100:0 – 95:5 gradient)] to give the *title compound* (57 mg, 87 %) as an orange solid.

Method L

4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidine-2-carboxylic acid (Example 124)

A solution of ethyl 4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidine-2-carboxylate (80 mg, 0.25 mmol) in MeOH (3 mL) was treated with 2M-NaOH (1 mL), stirred at room

temperature for 20 min, acidified with 1M-HCl, diluted with water and filtered to give the *title compound* (36 mg, 50 %) as a pale yellow solid.

Method M

Methyl 4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidine-2-carboxylate (Example 126)

A solution of ethyl 4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidine-2-carboxylate (100 mg, 0.31 mmol) in MeOH (5 mL) was refluxed for 2 h, cooled, diluted with water and filtered to give the *title compound* (73 mg, 74 %) as a cream solid.

Method N

Methanesulphonic acid 2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)hydrazide (Example 128)

A mixture of 2-hydrazinothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (110 mg, 0.4 mmol) and Et_3N (61 µL, 0.44 mmol) in THF (5 mL)was treated with methanesulphonyl chloride (31 µl, 0.4 mmol), stirred at room temperature for 20 min, poured into water (25 mL), extracted with EtOAc (2 x 5 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by chromatography [SiO_2: (EtOAc) to give the *title compound* (92 mg, 65 %) as an orange solid.

Method O

Acetic acid 2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)hydrazide (Example 130)

A solution of 2-hydrazinothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (83 mg, 0.3 mmol) in pyridine (5 mL)was treated with acetyl chloride (28 µl, 0.4 mmol), stirred at room temperature for 16 h, concentrated *in vacuo* and the resulting solid washed with water and EtOAc to give the *title compound* (42 mg, 44 %) as a yellow solid.

Method P

N-Allyl-2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)hydrazinecarboxamide (Example 131)

A mixture of 2-hydrazinothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (100 mg, 0.36 mmol) and THF (5 mL)was treated with allyl isocyanate (32 µl, 0.36 mmol), stirred at room temperature for 1h and filtered to give the *title compound* (88 mg, 68 %) as a yellow solid.

Method Q

N-(2-Dimethylaminoethyl)-4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-carboxamide (Example 134)

A mixture of 4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidine-2-carboxylic acid (290 mg, 1.0 mmol) and $SOCl_2$ (4 mL) was refluxed for 30 min, concentrated *in vacuo*, and treated with CH_2Cl_2 (10 mL), Et_3N (208 μL, 1.5 mmol) and N,N-dimethylethylenediamine (120 μL, 1.1 mmol). The reaction mixture was stirred at room temperature for 1 h, poured into sat. $NaHCO_3$, extracted with EtOAc (2 x 10 mL), dried ($MgSO_4$), concentrated *in vacuo* then triturated with EtOAc and filtered to give the *title compound* (234 mg, 65 %) as a cream solid.

Method R

2-Aminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (Example 110)

A mixture of 2-[N-(3,4-dimethoxybenzyl)]aminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (0.06 g, 0.15 mmol) and TFA (2 mL) was refluxed for 2 h, cooled, concentrated *in vacuo* to half its original volume, diluted with CH_2Cl_2 (50 mL),washed with saturated sodium bicarbonate solution (3 x 25 mL) then brine (25 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography [SiO_2; heptane-EtOAc (3 : 1)] to give the *title compound* (40 mg, 100 %) as a yellow solid.

Method S

N-Acetyl-N-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)acetamide (Example 137)

A mixture of 2-aminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (0.05 g, 0.19 mmol) and acetyl chloride (4.99 g, 0.063 mol) was refluxed for 5 h, cooled to room temperature, poured into water (50 mL) and extracted with EtOAc (3 x 30 mL). The organic phase was washed with saturated sodium bicarbonate solution (2 x 25 mL) and saturated brine (2 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to yield a brown solid which was purified by chromatography [SiO_2; heptane-EtOAc (2 : 1)] to give the *title compound* (40 mg, 60 %) as a yellow solid.

Method T

N-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)acetamide (Example 138)

A mixture of 2-aminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (0.07 g, 0.27 mmol), anhydrous pyridine (3 mL) and acetyl chloride (0.15 g, 1.88 mmol) was refluxed for 24 h, cooled to room temperature, poured into water (30 mL) and extracted with EtOAc (2 x 30 mL). The organic phase was washed with 1-M HCl (2 x 25 mL) and saturated brine (25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give a yellow solid which was purified by chromatography [SiO_2; heptane-EtOAc (2 : 1)] to give the *title compound* (50 mg, 58 %) as a yellow solid.

Method U

3-Methyl-N-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)butanamide (Example 150)

A solution of 2-(2-aminoethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (50 mg, 0.16 mmol) in CH_2Cl_2 (2 mL) was treated with triethylammonium methylpolystyrene carbonate (80 mg, 0.25 mmol) then isovaleryl chloride (30 mg, 0.25mmol) and shaken at room temperature for 6 h. The reaction mixture was treated with tris-(2-aminoethyl)amine polystyrene (0.20 g, 0.75 mmol), shaken at room temperature for 16 h, treated with polystyrene methylisocyanate (0.18 g, 0.25 mmol) and CH_2Cl_2 (2 mL), shaken for a further 6 h then filtered and concentrated *in vacuo* to give the *title compound* (35 mg, 55 %) as a yellow solid.

Method V

N-Allyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea (Example 159)

A solution of 2-(2-aminoethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (50 mg, 0.16 mmol) in anhydrous DMF (1 mL) was treated with allyl isocyanate (21 mg, 0.25 mmol), shaken at room temperature for 4 h, treated with tris-(2-aminoethyl)amine polystyrene (0.20 g, 0.75 mmol), shaken at 35°C for 16 h, treated with polystyrene methylisocyanate (0.22 g, 0.32 mmol) and DMF (2 mL) and shaken for a further 6 h. The reaction mixture was filtered and concentrated *in vacuo* to give the *title compound* (55 mg, 86 %) as a yellow solid.

Method W

N-Phenyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)thiourea (Example 164)

A solution of 2-(2-aminoethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (50 mg, 0.16 mmol) in anhydrous DMF (1 mL) was treated with phenyl isothiocyanate (33 mg, 0.25 mmol), shaken at room temperature for 2 h, poured into water (20 mL) and the resulting yellow precipitate was filtered and dried *in vacuo* to give the *title compound* (44 mg, 61 %) as a yellow solid.

Method X

2-Dimethylamino-N-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)acetamide hydrochloride (Example 169)

A solution of 2-aminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (0.15 g, 0.57 mmol) in anhydrous pyridine (6 mL) under argon at 0 °C was treated with N,N-dimethylglycinyl chloride hydrochloride (0.11 g, 0.69 mmol), warmed to room temperature, refluxed for 16 h, cooled, concentrated *in vacuo* and partitioned between 3-M HCl (25 mL) and EtOAc (25 mL). The aqueous phase was washed with EtOAc (25 mL), filtered through celite, basified to pH 12 with 10% aqueous sodium hydroxide and the resulting precipitate filtered and dried *in vacuo* to give a brown solid which was purified by chromatography [SiO_2; EtOAc-MeOH (100 : 0 to 85 : 15)]. The resulting yellow solid was dissolved in CH_2Cl_2 (5 mL), treated with 1-M HCl in ether (0.25 mL) and the resulting precipitate filtered and dried *in vacuo* to give the *title compound* (32 mg, 11 %) as a yellow solid.

Method Y

N,N'-Bis(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea (Example 170)

A solution of 2-(2-aminoethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (0.10 g, 0.33 mmol) in anhydrous DMF (4 mL) under argon was treated with 1,1-carbonyldiimidazole (0.05 g, 0.33 mmol), stirred for 2 h, treated with 2-(2-aminoethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone (0.10 g, 0.33 mmol), stirred at room temperature for 4 h and then at 60 °C for 16 h, cooled, poured into water (25 mL) and the resulting orange suspension filtered and dried *in vacuo* to give the *title compound* (0.13 g, 31 %) as an orange solid.

Method Z

4-Chloro-2-methylthieno[3,2-d]pyrimidine

A suspension of 4-hydroxy-2-methylthieno[3,2-d]pyrimidine (0.631 g, 3.8 mmol) in $POCl_3$ (10 mL, 400 mmol) was refluxed for 4 h, concentrated *in vacuo*, treated with saturated $NaHCO_3$ (20 mL), extracted with EtOAc (2 x 20 mL) and the combined extracts dried ($MgSO_4$) and concentrated *in vacuo* to give the *title compound* (0.645 g, 92 % as a pale yellow solid: mp 82 – 84 °C; IR ν_{max} (Nujol)/cm^{-1} 3073, 2925, 2855, 1566, 1515, 1460, 1378, 1344, 1307, 894 and 795; NMR δ_H (400 MHz, DMSO-d_6) 3.41 (3H, s), 7.72 (1H, d, *J* 5.0 Hz) and 8.61 (1H, d, *J* 5.0 Hz).

4-Chloro-2-*n*-propylthieno[3,2-d]pyrimidine

This was prepared from 4-hydroxy-2-*n*-propylthieno[3,2-d]pyrimidine by method Z and the *title compound* (0.91 g, 78 %) isolated as a pale yellow oil: IR ν_{max} (Nujol)/cm^{-1} 2963, 2932, 1564, 1514, 1459, 1338, 1322, 1100 and 799; NMR δ_H (400 MHz, $CDCl_3$) 1.04 (3H, t, *J* 7.5 Hz), 1.93 (2H, m), 3.04 (2H, t, *J* 7.5 Hz), 7.55 (1H, d, *J* 5.5 Hz) and 8.02 (1H, d, *J* 5.5 Hz).

Ethyl 4-chlorothieno[3,2-d]pyrimidine-2-carboxylate

This was prepared from ethyl 4-oxothieno[3,2-d]pyrimidine-2-carboxylate by method Z and the crude *title compound* (757 mg, quantitative) isolated as an off-white solid: IR ν_{max} (Nujol)/cm^{-1} 3091, 3061, 2925, 2854, 1732, 1547, 1456, 1325 and 1196; NMR δ_H (400 MHz, $CDCl_3$) 1.49 (3H, t, *J* 7.1 Hz), 4.59 (2H, q, *J* 7.1 Hz), 7.80 (1H, d, *J* 5.5 Hz), and 8.17 (1H, d, *J* 5.5 Hz).

Method AA

Ethyl 4-oxothieno[3,2-d]pyrimidine-2-carboxylate

A mixture of 3-aminothiophene-2-carboxamide (1.23 g, 8.65 mmol) and EtOH (25 mL) was treated with NaOEt (1.2 g, 17.3 mmol) and diethyloxalate (2.3 mL, 17.3 mmol), refluxed for 18 h, cooled, concentrated *in vacuo*, treated with water, acidified with HOAc and filtered to give the *title compound* (1.43 g, 74 %) as a cream solid: IR ν_{max} Nujol)/cm^{-1} 3180, 3119, 3078, 3006, 2955, 2924, 2854, 1737, 1667, 1651, 1300 and 1176; NMR δ_H (400 MHz, DMSO) 1.37 (3H, t, *J* 7.0 Hz), 4.40 (2H, q, *J* 7.0 Hz), 7.58 (1H, d, *J* 5.0 Hz), 8.30 (1H, d, *J* 5.1 Hz), and 12.92 (1H, s).

Experimental data for Examples 1 – 170 are provided in Table 2.

HPLC is carried out using the following conditions: Column. Supelcosil ABZ$^+$ (170 x 4.6 mm), particle size 5 μM, mobile phase MeOH : 10 mM aq NH_4OAc (8:2), (9:1) or (100:0) (specified in Table 2), flow rate 1.0 mL/min., detection wavelength λ = 230 nM (unless otherwise stated), retention times are provided in Table 2.

Table 2

Example	Method	Yield(%)	Physical Data
1	A	43	mp 116 - 118 °C; IR ν_{max} (Nujol)/cm^{-1} 3138, 3103, 3088, 2924, 1635, 1507, 1443, 1422, 1282, 1245, 1189, 1165, 1092, 760, 734 and 602; NMR δ_H (400 MHz, $CDCl_3$) 7.42 (1H, m), 7.78 (1H, d, *J* 5.5 Hz), 8.06 (1H, m), 8.42 (1H, d, *J* 5.5 Hz) and 8.48 (2H, d, *J* 1.5 Hz); Anal. Calcd for $C_{14}H_7F_3N_2OS$: C, 54.55; H, 2.19; N, 9.08. Found: C, 54.41; H, 2.29; N, 8.99.
2	A	53	mp 173 - 175 °C; IR ν_{max} (Nujol)/cm^{-1} 3091, 1632, 1412, 1245, 1195, 1175, 1147, 1056, 771 and 739; NMR δ_H (400 MHz, $CDCl_3$) 7.30 (1H, s), 7.79 (1H, d, *J* 5.5 Hz), 7.92 (1H, m), 8.41 (1H, d, *J* 5.5 Hz) and 8.77 (1H, m); Anal. Calcd for $C_{12}H_5F_3N_2OS_2$: C, 45.86; H, 1.60; N, 8.91; S, 20.40. Found: C, 45.90; H, 1.67; N, 8.84; S, 20.62.
3	A	75	mp 164 - 166 °C; IR ν_{max} (Nujol)/cm^{-1} 3081, 2924, 1647, 1462, 1448, 1235, 1182, 1140, 824, 730 and 669; NMR δ_H (400 MHz, $CDCl_3$) 7.43 (1H, m), 7.79 (1H, d, *J* 5.6 Hz), 8.06 (1H, m), 8.39 (1H, d, *J* 5.5 Hz) and 9.48 (1H, m); Anal. Calcd for $C_{12}H_5F_3N_2OS_2$: C, 45.86; H, 1.60; N, 8.91. Found: C, 45.78; H, 1.63; N, 8.83.
4	A	40	mp 190 - 192 °C; IR ν_{max} (Nujol)/cm^{-1} 3167, 3148, 3089, 1639, 1463, 1441, 1177, 1153, 1137, 1086, 1046, 1016, 912, 820, 791, 772 and 736; NMR δ_H (400 MHz, $CDCl_3$) 6.74 (1H, m), 7.79 (1H, d, *J* 5.5 Hz), 7.88 (1H, s), 8.41 (1H, d, *J* 5.5 Hz) and 8.63 (1H, d, *J* 3.0 Hz); Anal. Calcd for $C_{12}H_5F_3N_2O_2S$: C, 48.33; H, 1.69; N, 9.39. Found: C, 48.19; H, 1.75; N, 9.25.
5	A	17	mp 136 - 138 °C; IR ν_{max} (Nujol)/cm^{-1} 3170, 3101, 3084, 1640, 1525, 1512, 1465, 1438, 1376, 1300, 1269, 1202, 1178, 1157, 1137, 1092, 998, 917, 873, 787, 778, 747, 735 and 598; NMR δ_H (400 MHz, $CDCl_3$) 6.92 (1H, m), 7.56 (1H, s), 7.79 (1H, d, *J* 6 Hz), 8.41 (1H, d, *J* 7 Hz) and 9.30 (1H, s); Anal. Calcd for $C_{12}H_5F_3N_2O_2S$: C, 48.33; H, 1.69; N, 9.39. Found: C, 48.40; H, 1.77; N, 9.22.

6	A	8	mp 230 – 233 °C; IR ν_{max} (Nujol)/cm^{-1} 3288, 3087, 1608, 1535, 1465, 1440, 1381, 1199, 1184, 1143, 1049 and 765; NMR δ_H (400 MHz, $CDCl_3$) 6.45 (1H, m), 7.30 (1H, m), 7.50 (0.5H, br s), 7.78 (1H, d, *J* 5.5 Hz), 8.41 (1H, br m) and 9.70 (0.5H, br s); Anal. Calcd for $C_{12}H_6F_3N_3OS$: C, 48.49; H, 2.03; N, 14.13. Found: C, 48.23; H, 2.06; N, 13.96.
7	A	36	mp 140 - 142 °C; IR ν_{max} (Nujol)/cm^{-1} 3113, 3077, 1679, 1461, 1440, 1410, 1378, 1363, 1273, 1247, 1203, 1177, 1151, 933, 815, 740 and 772; NMR δ_H (400 MHz, $CDCl_3$) 7.84 (1H, d, *J* 20 Hz), 8.34 (2H, d, *J* 5.5 Hz), 8.38 (1H, d, *J* 20 Hz) and 8.68 (2H, d, *J* 5.5 Hz).
8	A	53	mp 122 - 123 °C; IR ν_{max} (Nujol)/cm^{-1} 3119, 3058, 1676, 1590, 1524, 1463, 1440, 1362, 1235, 1212, 1178, 1139, 1021, 931, 820, 747 and 650; NMR δ_H (400 MHz, $CDCl_3$) 7.4 – 7.6 (3H, m), 7.68 (1H, dd, *J* 7.0, 1.0 Hz), 7.81 (1H, d, *J* 6.0 Hz) and 8.45 (1H, d, *J* 7.0 Hz); Anal. Calcd for $C_{14}H_6ClF_3N_2OS$: C, 49.06; H, 1.76; N, 8.17. Found: C, 49.28; H, 1.85; N, 8.11.
9	A	49	mp 128 - 130 °C; IR ν_{max} (Nujol)/cm^{-1} 3107, 3082, 1651, 1562, 1529, 1465, 1440, 1378, 1362, 1276, 1227, 1178, 1140, 1099, 1029, 847, 823, 773, 752, 731, 694, 672, 657 and 604; NMR δ_H (400 MHz, $CDCl_3$) 7.52 (1H, t, *J* 8 Hz), 7.68 (1H, dd, *J* 2.5, 1.0 Hz), 7.81 (1H, d, *J* 5.5 Hz), 8.42 (1H, d, *J* 5.5 Hz), 8.46 (1H, m) and 8.48 (1H, d, *J* 1.0 Hz); Anal. Calcd for $C_{14}H_6ClF_3N_2OS$: C, 49.06; H, 1.76; N, 8.17. Found: C, 48.90; H, 1.83; N, 8.00.
10	A	41	mp 147 - 149 °C; IR ν_{max} (Nujol)/cm^{-1} 3105, 3085, 1650, 1562, 1535, 1443, 1379, 1361, 1280, 1225, 1178, 1100, 944, 817, 777, 719, 692 and 662; NMR δ_H (400 MHz, $CDCl_3$) 7.68 (1H, d, *J* 1.5 Hz), 7.83 (1H, d, *J* 5.5 Hz), 8.44 (1H, d, *J* 5.5 Hz), and 8.47 (2H, d, *J* 1.5 Hz); Anal. Calcd for $C_{14}H_5Cl_2F_3N_2OS$: C, 44.58; H, 1.34; N, 7.42. Found: C, 44.52; H, 1.33; N, 7.30.
11	A	30	mp 116 - 118 °C; IR ν_{max} (Nujol)/cm^{-1} 3118, 3084, 2951, 1665, 1543, 1520, 1477, 1458, 1440, 1380, 1276, 1234, 1194, 1176, 1142, 1093, 930, 745 and 738; NMR δ_H (400 MHz, $CDCl_3$) 2.51 (3H, s), 7.3 – 7.4 (2H, m), 7.52 (1H, t, *J* 7.5 Hz), 7.78 (2H, m) and 8.41 (1H, d, *J* 6.0 Hz); Anal. Calcd for $C_{15}H_9F_3N_2OS$: C, 55.90; H, 2.81; N, 8.69. Found: C, 55.94; H, 2.83; N, 8.69.
12	A	17	0.12 g, 17 % mp 165 - 167 °C; IR ν_{max} (Nujol)/cm^{-1} 3081, 1638, 1512, 1458, 1440, 1413, 1374, 1324, 1230, 1201, 1174, 1143, 933, 819, 803, 777, 760 and 739; NMR δ_H (400 MHz, $CDCl_3$) 7.14 (1H, d, *J* 5.5 Hz), 7.90 (1H, d, *J* 3.5 Hz), 8.42 (1H, d, *J* 3.5 Hz) and 8.47 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{12}H_4ClF_3N_2OS_2$: C, 41.33; H, 1.16; N, 8.03. Found: C, 41.42; H, 1.23; N, 7.97.

13	A	34	mp 161 - 163 °C; IR ν_{max} (Nujol)/cm^{-1} 3108, 3079, 1629, 1545, 1443, 1240, 1203, 1174, 1140, 1050, 933, 820, 778 and 762; NMR δ_H (400 MHz, $CDCl_3$) 2.64 (3H, s), 6.98 (1H, m), 7.78 (1H, d, *J* 8.0 Hz), 8.39 (1H, d, *J* 8.0 Hz) and 8.71 (1H, m); Anal. Calcd for $C_{13}H_7F_3N_2OS_2$: C, 47.56; H, 2.15; N, 8.53. Found: C, 47.89; H,2.28 ; N, 8.50.
14	A	41	mp 196 - 197 °C; IR ν_{max} (Nujol)/cm^{-1} 3104, 3086, 3061, 1655, 1526, 1464, 1396, 1369, 1331, 1265, 1237, 1211, 1173, 1155, 937, 921, 804, 777 and 738; NMR δ_H (400 MHz, $CDCl_3$) 7.85 (1H, d, *J* 5.5 Hz), 7.94 (1H, d, *J* 3.0 Hz), 8.31 (1H, d, *J* 3.0 Hz) and 8.48 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{11}H_4F_3N_3OS_2$: C, 41.90; H, 1.28; N, 13.32. Found: C, 41.67; H, 1.34; N, 13.17.
15	A	14	mp 221 - 223 °C; IR ν_{max} (Nujol)/cm^{-1} 3140, 3109, 3064, 2925, 2834, 1649, 1611, 1536, 1465, 1438, 1295, 1203, 1171, 1159, 1141, 1094, 1035, 917, 832, 814, 774, 753 and 733; NMR δ_H (400 MHz, $CDCl_3$) 7.40 (1H, t, *J* 5.5 Hz), 7.59 (1H, t, *J* 5.5 Hz), 7.68 (1H, d, *J* 8.0 Hz), 7.81 (1H, d, *J* 5.5 Hz), 7.89 (1H, d, *J* 8.0 Hz), 8.43 (1H, d, *J* 5.5 Hz) and 8.95 (1H, s); Anal. Calcd for $C_{16}H_7F_3N_2O_2S$: C, 55.18; H, 2.03; N, 8.04. Found: C, 55.16; H, 2.03; N, 7.98.
16	B	25	mp 142 - 143 °C; IR ν_{max} (Nujol)/cm^{-1} 3096, 2249, 1533, 1526, 1456, 1142, 1202, 1176, 1142, 731, 706 and 698; NMR δ_H (400 MHz, $CDCl_3$) 5.64 (1H, s), 7.4 (3H, m), 7.6 (2H, m), 7.71 (1H, d, *J* 8.0 Hz) and 8.14 (1H, d, *J* 8.0 Hz).
17	B	41	mp 157 - 159 °C; IR ν_{max} (Nujol)/cm^{-1} 3113, 3098, 2251, 1554, 1525, 1483, 1442, 1439, 1275, 1201, 1177, 819, 771, 736 and 681; NMR δ_H (400 MHz, $CDCl_3$) 5.79 (1H, s), 7.09 (1H, m), 7.38 (1H, m), 7.61 (1H, m), 7.71 (1H, d, *J* 5.5 Hz) and 8.17 (1H, d, *J* 8.0 Hz); Anal. Calcd for $C_{13}H_6F_3N_3S_2$: C, 48.00; H, 1.86; N, 12.91; S, 19.71. Found: C, 48.29; H, 1.95; N, 12.76; S, 19.70.
18	B	12	IR ν_{max} (Nujol)/cm^{-1} 3118, 3100, 2184, 1630, 1589, 1551, 1463, 1377, 1283, 1187, 1176, 1145, 1136, 800, 768 and 740; NMR δ_H (400 MHz, $CDCl_3$) 5.31 (1H, s), 6.94 (1H, m), 7.55 (1H, d, *J* 8.0 Hz), 7.66 (1H, d, *J* 8.9 Hz), 7.84 (1H, m), 7.94 (1H, d, *J* 6.0 Hz) and 7.99 (1H, d, *J* 5.0 Hz).
19	B	59	NMR δ_H (400 MHz, $CDCl_3$) 1.24 (3H, t, *J* 8.0 Hz), 4.2 – 4.4 (1H, m), 5.48 (1H, s), 7.38 (3H, m), 7.50 (2H, m), 7.62 (1H, d, *J* 5.5 Hz) and 8.02 (1H, d, *J* 5.5 Hz).
20	C	36	NMR δ_H (400 MHz, $CDCl_3$) 3.31 (1H, br s), 4.2 (1H, m), 4.70 (2H, s), 7.2 – 7.4 (5H, m), 7.63 (1H, d, *J* 5.5 Hz) and 8.02 (1H, d, *J* 5.5 Hz).
21	D	27	NMR δ_H (400 MHz, $CDCl_3$) 4.40 (1H, m), 6.10 (1H, m), 7.35 (3H, m), 7.50 (2H, m), 7.66 (1H, d, *J* 8.0 Hz) and 8.10 (1H, d, *J* 8.0 Hz).
22	E	98	IR ν_{max} (Nujol)/cm^{-1} 3199, 3108, 1547, 1522, 1458, 1399, 1261, 1201, 1177, 1146, 813, 740 and 718; NMR δ_H (400 MHz, $CDCl_3$) 7.35 – 7.55 (5H, m), 7.73 – 7.77 (1H, m) and 8.20 – 8.26 (2H, m).

23	E	95	IR ν_{max} (Nujol)/cm^{-1} 3186, 2955, 1544, 1523, 1416, 1385, 1256, 1201, 1169, 1142, 1038, 813, 786 and 740; NMR δ_H (400 MHz, $CDCl_3$) 7.19 (0.5H, m), 7.30 – 7.50 (1.5H, m), 7.70 – 7.90 (1.5H, m), 8.10 – 8.30 (2H, m) and 8.70 (0.5H, br s).
24	A	12	mp 188 - 190 °C; IR ν_{max} (Nujol)/cm^{-1} 3111, 3051, 2924, 1627, 1523, 1494, 1463, 1407, 1372, 1255, 1226, 1216, 1195, 1046, 970, 882, 786, 747 and 596; NMR δ_H (400 MHz, $CDCl_3$) 2.54 (3H, s), 7.29 (1H, t, *J* 5.5 Hz), 7.88 (1H, d, *J* 5.5 Hz), 7.97 (1H, s) and 8.69 (1H, d, *J* 4.0 Hz); Anal. Calcd for $C_{12}H_7ClN_2OS_2$: C, 48.90; H, 2.39; N, 9.50. Found: C, 48.52; H, 2.36; N, 9.14.
25	A	46	mp 128 - 130 °C; IR ν_{max} (Nujol)/cm^{-1} 3115, 3096, 2854, 1655, 1583, 1530, 1461, 1439, 1415, 1360, 1268, 1237, 1207, 1196, 1172, 1015, 934, 833, 812, 758, 737 and 688; NMR δ_H (400 MHz, $CDCl_3$) 7.51 (1H, m), 7.84 (1H, d, *J* 5.5 Hz), 8.46 (1H, d, *J* 5.5 Hz), 8.70 – 8.90 (2H, m) and 9.71 (1H, d, *J* 1.5 Hz); Anal. Calcd for $C_{13}H_6F_3N_3OS$: C, 50.49; H, 1.96, N, 13.58. Found: C, 50.49; H, 1.88; N, 13.51.
26	A	32	mp 165 - 169 °C; IR ν_{max} (Nujol)/cm^{-1} 3092, 3068, 2924, 1688, 1586, 1546, 1522, 1465, 1438, 1364, 1287, 1261, 1237, 1178, 1139, 1033, 936, 824, 808, 780, 751, 739, 694, 686 and 600; NMR δ_H (400 MHz, $CDCl_3$) 7.60 (1H, m), 7.81 (1H, d, *J* 5.5 Hz), 7.99 (1H, m), 8.01 (1H, d, *J* 2.4 Hz), 8.38 (1H, d, *J* 5.5 Hz) and 8.84 (1H, m); Anal. Calcd for $C_{13}H_6F_3N_3OS$: C, 50.49; H, 1.96, N, 13.58. Found: C, 50.61; H, 1.99; N, 13.38.
27	A	65	mp 155 - 157 °C; IR ν_{max} (Nujol)/cm^{-1} 3106, 3092, 3076, 2955, 2854, 1636, 1596, 1567, 1535, 1508, 1464, 1440, 1424, 1360, 1288, 1266, 1240, 1173, 1138, 1018, 932, 848, 777, 738, 654 and 600; NMR δ_H (400 MHz, $CDCl_3$) 3.95 (3H, s), 7.07 (2H, d, *J* 12.0 Hz), 7.79 (1H, d, *J* 5.5 Hz), 8.40 (1H, d, *J* 5.5 Hz) and 8.62 (2H, d, *J* 12.0 Hz); Anal. Calcd for $C_{15}H_9F_3N_2O_2S$: C, 53.26; H, 2.68, N, 8.28. Found: C, 53.33; H, 2.62; N, 8.27.
28	A	48	mp 162.2 – 163.1 °C; IR ν_{max} (Nujol)/cm^{-1} 3095, 3069, 2924, 2855, 1658, 1531, 1517, 1354, 1252 and 1208; NMR δ_H (400 MHz, $CDCl_3$) 7.55 – 7.59 (2H, m), 7.62 (1H, d, *J* 5.5 Hz), 7.67 – 7.71 (1H, m), 8.31 (1H, d, *J* 5.5 Hz) and 8.40 – 8.43 (2H, m);); Anal. Calcd for $C_{13}H_7ClN_2OS$: C, 56.84; H, 2.57, N, 10.19. Found: C, 56.79; H, 2.34; N, 10.13.
29	A	54	mp 127 - 129 °C; IR ν_{max} (Nujol)/cm^{-1} 3099, 3071, 2923, 1645, 1601, 1530, 1460, 1440, 1392, 1358, 1279, 1232, 1210, 1184, 1169, 1132, 1096, 1018, 932, 843, 834, 778, 766, 735, 649, 596 and 562; NMR δ_H (400 MHz, $CDCl_3$) 2.48 (3H, s), 7.43 (2H, d, *J* 6.0 Hz), 7.79 (1H, d, *J* 5.5 Hz), 8.38 (1H, d, *J* 5.5 Hz) and 8.45 (2H, d, *J* 6.0 Hz); Anal. Calcd for $C_{15}H_9F_3N_2OS$: C, 55.90; H, 2.81, N, 8.69. Found: C, 56.13; H, 2.74; N, 8.69.

30	A	59	mp 127 - 128 °C; IR ν_{max} (Nujol)/cm^{-1} 3108, 3093, 3077, 2924, 1645, 1583, 1529, 1459, 1443, 1405, 1387, 1360, 1284, 1230, 1196, 1177, 1148, 1138, 1090, 1011, 933, 828, 813, 779, 770, 741, 645, 562 and 547; NMR δ_H (400 MHz, $CDCl_3$) 7.59 (2H, d, *J* 11.0 Hz), 7.77 (1H, d, *J* 5.5 Hz), 8.43 (1H, d, *J* 5.5 Hz) and 8.53 (2H, d, *J* 11.0 Hz); Anal. Calcd for $C_{14}H_6ClF_3N_2OS$: C, 49.06; H, 1.76; N, 8.17. Found: C, 48.93; H, 1.75; N, 8.17.
31	A	17	mp 185 - 186 °C; IR ν_{max} (Nujol)/cm^{-1} 3104, 3077, 3053, 2955, 2925, 1675, 1600, 1531, 1519, 1442, 1345, 1318, 1281, 1234, 1191, 1176, 1145, 1031, 934, 823, 810 and 740; NMR δ_H (400 MHz, $CDCl_3$) 7.85 (1H, d, *J* 5.5 Hz), 8.40 – 8.60 (3H, m) and 8.67 (2H, d, *J* 11.0 Hz); Anal. Calcd for $C_{14}H_6F_3N_3O_3S$: C, 47.60; H, 1.71; N, 11.89. Found: C, 47.47; H, 1.70; N, 11.69.
32	A	39	mp 131 - 133 °C; IR ν_{max} (Nujol)/cm^{-1} 3106, 3079, 2924, 1649, 1598, 1530, 1480, 1462, 1439, 1384, 1360, 1281, 1247, 1190, 1142, 1098, 1047, 943, 821, 770, 755, 736, 678, 666 and 604; NMR δ_H (400 MHz, $CDCl_3$) 2.42 (3H, s), 7.40 – 7.60 (2H, m), 7.79 (1H, d, *J* 5.5 Hz), 8.20 – 8.30 (2H, m) and 8.39 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{15}H_9F_3N_2OS$: C, 55.90; H, 2.81, N, 8.69. Found: C, 55.87; H, 2.79; N, 8.69.
33	A	14	mp 117 - 120 °C; IR ν_{max} (Nujol)/cm^{-1} 3082, 3042, 1691, 1606, 1572, 1528, 1448, 1394, 1357, 1276, 1255, 1231, 1210, 1168, 1080, 1025, 930, 902, 833, 815, 793, 766, 739, 695 and 684; NMR δ_H (400 MHz, $CDCl_3$) 7.16 (1H, t, *J* 8.0 Hz), 7.35 (1H, d, *J* 8.0 Hz), 7.45 – 7.55 (1H, m), 7.83 (1H, d, *J* 5.5 Hz) and 8.42 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{14}H_5ClF_4N_2OS$: C, 46.62; H, 1.40, N, 7.76. Found: C, 46.59; H, 1.42; N, 7.71.
34	B	50	mp 240 - 242 °C; IR ν_{max} (Nujol)/cm^{-1} 3089, 2925, 2180, 1614, 1590, 1557, 1501, 1452, 1416, 1377, 1296, 1257 and 1234; NMR δ_H (400 MHz, $CDCl_3$) 1.50 (3H, t, *J* 7.5 Hz), 2.90 (2H, q, *J* 7.5 Hz), 6.99 – 7.02 (1H, m), 7.28 (1H, d, *J* 5.5 Hz), 7.61 – 7.63 (1H, m), 7.69 – 7.73 (1H, m), 7.76 (1H, d, *J* 5.5 Hz) and 8.37 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{15}H_{12}N_4S$: C, 64.27; H, 4.31, N, 19.98. Found: C, 64.53; H, 4.31; N, 19.96.
35	A	66	mp 111 - 112 °C; IR ν_{max} (Nujol)/cm^{-1} 2925, 1632, 1621, 1550, 1498, 1463, 1408, 1378, 1364, 1342, 1296, 1429, 1190 and 1050; NMR δ_H (400 MHz, $CDCl_3$) 1.58 (3H, t, *J* 7.5 Hz), 3.29 (2H, q, *J* 7.5 Hz), 7.24 – 7.27 (1H, m), 7.57 (1H, d, *J* 5.5 Hz), 7.86 (1H, dd, *J* 4.0, 1.0 Hz), 8.18 (1H, d, *J* 5.5 Hz) and 8.63 (1H, dd, *J* 4.0, 1.0 Hz); Anal. Calcd for $C_{13}H_{10}N_2OS_2$: C, 56.91; H, 3.67; N, 10.21. Found: C, 56.96; H, 3.64; N, 10.23.
36	D	64	mp 147 - 149 °C; IR ν_{max} (Nujol)/cm^{-1} 3134, 2924, 1535, 1460, 1381, 1359, 1310, 1264, 1224, 1138, 1106 and 1097; NMR δ_H (400 MHz, $CDCl_3$) 1.48 (3H, t, *J* 7.5 Hz), 5.52 (1H, br s), 6.23 (1H, br s), 7.00 (1H, dd, *J* 3.5, 1.5 Hz), 7.23 (1H, d, *J* 3.5 Hz), 7.32 (1H, dd, *J* 4.0, 1.0 Hz), 7.50 (1H, d *J* 5.5 Hz) and 7.91 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{13}H_{12}N_2OS_2$: C, 56.50; H, 4.38; N, 10.13. Found: C, 56.62; H, 4.40; N, 10.07.

37	F	74	mp 144 – 146 °C; IR ν_{max} (Nujol)/cm^{-1} 3110, 3051, 3009, 1630, 1562, 1548, 1497, 1467, 1405, 1381, 1341, 1243, 1061, 1044, 852, 802, 761, 737 and 609; NMR δ_H (400 MHz, $CDCl_3$) 2.43 (3H, s), 4.27 (3H, s), 7.28 (1H, m), 7.79 (1H, s), 7.85 (1H, m), and 8.59 (1H, m); Anal. Calcd for $C_{13}H_{10}N_2O_2S_2$; C, 53.78; H, 3.47; N, 9.64. Found C, 53.25; H, 3.52; N, 9.47.
38	F	68	mp 156-158 °C; NMR δ_H (400 MHz, $CDCl_3$) 2.39 (3H, s), 3.4 (6H, s), 7.22 (1H, m), 7.59 (1H, s), 7.82 (1H, m), and 8.42 (1H, m).
39	F	70	mp 144-166 °C; IR ν_{max} (Nujol/cm^{-1}) 3067, 2923, 1625, 1566, 1499, 1463, 1410, 1377, 1309, 1249, 1214, 1045, 759, and 716; NMR δ_H (400 MHz, $CDCl_3$) 2.49 (3H, s), 2.80 (3H, s), 7.24 (1H, m), 7.51 (1H, s), 7.83 (1H, m) and 8.58 (1H, m).
40	F	76	mp 116.5 – 117 °C; IR ν_{max} (Nujol)/cm^{-1} 3051, 2924, 2854, 1657, 1559, 1355 and 733; NMR δ_H (400 MHz, $CDCl_3$) 3.27 (6H, s), 7.28 (1H, d, *J* 5.5 Hz), 7.48 – 7.52 (2H, m), 7.60 – 7.64 (1H, m), 7.97 (1H, d, *J* 5.5 Hz) and 8.35 – 8.38 (2H, m).
41	D	63	mp 157 - 158°C; NMR δ_H (400 MHz, $CDCl_3$) 4.45 (1H, br s), 6.39 (1H, s), 6.98 (1H, m), 7.22 (1H, m), 7.34 (1H, m), 7.70 (1H, d, *J* 5.5 Hz) and 8.13 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{12}H_7F_3N_2OS_2$; C, 45.57; H, 2.23; N, 8.85. Found C, 45.79; H, 2.25; N, 8.82.
42	A	18	mp 201-202 °C; NMR δ_H (400 MHz, $CDCl_3$) 2.79 (3H, s), 7.08 (1H, d, *J* 5.5 Hz), 7.6 - 7.8 (2H, m) and 8.39 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{13}H_7F_3N_2OS_2$; C, 47.56; H, 2.15; N, 8.53. Found C, 47.84; H, 2.17; N, 8.53.
43	A	29	mp 200 - 201 °C; NMR δ_H (400 MHz, $CDCl_3$) 2.52 (3H, s), 6.37 (1H, m), 7.78 (1H, d, *J* 5.5 Hz), 8.38 (1H, d, *J* 5.5 Hz) and 8.41 (1H, d, *J* 4.8 Hz); Anal. Calcd for $C_{13}H_7F_3N_2O_2S$; C, 50.00; H, 2.26; N, 8.97. Found C, 50.26; H, 2.26; N, 8.88.
44	A	46	mp 190.5 – 191 °C; IR ν_{max} (Nujol)/cm^{-1} 3102, 3086, 2925, 1619, 1526, 1521, 1463, 1410, 1378, 1364, 1256, 765 and 734; NMR δ_H (400 MHz, $CDCl_3$) 7.28 (1H, dd, *J* 4.6, 3.9 Hz), 7.60 (1H, d, *J* 5.5 Hz), 7.89 (1H, d, *J* 4.9 Hz), 8.30 (1H, d, *J* 5.5 Hz) and 8.71 (1H, d, *J* 4.0 Hz); Anal. Calcd for $C_{11}H_5ClN_2OS_2$: C, 47.06; H, 1.80, N, 9.97. Found: C, 46.84; H, 1.84; N, 9.87.
45	F	76	mp 203.1 – 204.2 °C; IR ν_{max} (Nujol)/cm^{-1} 3085, 3065, 2924, 2854, 1637, 1573, 1537, 1506, 1462, 1411, 1373, 1251, 1048, 801, 765 and 717; NMR δ_H (400 MHz, $CDCl_3$) 3.39 (6H, s), 7.23 (1H, dd, *J* 4.6, 4.0 Hz), 7.27 (1H, d, *J* 5.5 Hz), 7.81 (1H, d, *J* 4.6 Hz), 7.99 (1H, d, *J* 5.5 Hz) and 8.48 (1H, d, *J* 4.0 Hz); Anal. Calcd for $C_{10}H_{11}N_3OS_2$: C, 53.96; H, 3.83, N, 14.51. Found: C, 53.77; H, 3.78; N, 14.36.
46	A	45	mp 180-182 °C; NMR δ_H (400 MHz, $CDCl_3$) 7.26 (1H, m), 7.80 (1H, d, *J* 5.5 Hz) and 8.3 - 8.4 (2H, m); Anal. Calcd for $C_{12}H_4F_3BrN_2OS_2$; C, 36.66; H, 1.03; N, 7.12. Found C, 36.80; H, 1.15; N, 7.05.

47	F	90	mp 178.4 – 178.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3107, 3081, 2925, 2855, 1624, 1545, 1462, 1409, 1352, 1332 and 1230; NMR δ_H (400 MHz, $CDCl_3$) 4.24 (3H, s), 7.25 (1H, dd, *J* 5.1, 4.0 Hz), 7.44 (1H, d, *J* 5.5 Hz), 7.84 (1H, d, *J* 5.1 Hz), 8.17 (1H, d, *J* 5.5 Hz) and 8.60 (1H, d, *J* 4.0 Hz); Anal. Calcd for $C_{12}H_8N_2O_2S_2$: C, 52.16; H, 2.92, N, 10.13. Found: C, 52.03; H, 3.00; N, 10.03.
48	F	90	mp 189.7 – 190.6 °C; IR ν_{max} (Nujol)/cm^{-1} 3095, 3079, 2925, 2855, 1633, 1539, 1409, 1371, 1261, 1219 and 759; NMR δ_H (400 MHz, $CDCl_3$) 2.79 (3H, s), 7.26 (1H, dd, *J* 5.0, 4.0 Hz), 7.48 (1H, d, *J* 5.5 Hz), 7.85 (1H, d, *J* 5.0 Hz), 8.16 (1H, d, *J* 5.5 Hz) and 8.60 (1H, d, *J* 4.0 Hz); Anal. Calcd for $C_{12}H_8N_2OS_3$: C, 49.29; H, 2.76, N, 9.58. Found: C, 49.31; H, 2.76; N, 9.53.
49	F	68	mp 166.1 – 166.6 °C; IR ν_{max} (Nujol)/cm^{-1} 3287, 3104, 2925, 2855, 1634,1589, 1462 and 1363; NMR δ_H (400 MHz, $CDCl_3$) 1.36 (3H, t, *J* 7.0 Hz), 3.68 (2H, q, *J* 7.0 Hz), 5.22 (1H, s), 7.21 – 7.26 (2H, m), 7.81 (1H, d, *J* 5.1 Hz), 8.01 (1H, d, *J* 5.5 Hz) and 8.51 (1H, d, *J* 4.0 Hz); Anal. Calcd for $C_{13}H_{11}N_3OS_2$: C, 53.96; H, 3.83, N, 14.51. Found: C, 53.82; H, 3.62; N, 14.41.
50	F	32	mp 153.6 – 154.1 °C; IR ν_{max} (Nujol)/cm^{-1} 3258, 3101, 3024, 2925, 2855, 1635, 1598, 1407, 1366, 1350,764 and 724; NMR δ_H (400 MHz, $CDCl_3$) 4.87 (2H, d, *J* 5.9 Hz), 5.59 (1H, t, *J* 5.6 Hz), 7.17 (1H, t, *J* 4.2 Hz), 7.25 – 7.34 (2H, m), 7.37 (2H, t, *J* 7.7 Hz), 7.45 (2H, d, *J* 7.7 Hz), 7.76 (1H, d, *J* 5.1 Hz), 8.04 (1H, d, *J* 5.5 Hz) and 8.40 (1H, d, *J* 5.1 Hz); Anal. Calcd for $C_{18}H_{13}N_3OS_2$: C, 61.52; H, 3.73, N, 11.95. Found: C, 61.47; H, 3.52; N, 11.88.
51	F	57	mp 162.8 – 163.3 °C; IR ν_{max} (Nujol)/cm^{-1} 3300 – 3100, 2925, 2855, 1632, 1576, 1409, 1368, 764 and 726; NMR δ_H (400 MHz, $CDCl_3$) 2.62 – 3.08 (1H, s), 3.81 (2H, q, *J* 5.5 Hz), 3.96 (2H, q, *J* 5.2 Hz), 5.67 (1H, t, *J* 5.6 Hz), 7.21 – 7.25 (2H, m), 7.81 (1H, d, *J* 4.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.48 (1H, d, *J* 4.0 Hz); Anal. Calcd for $C_{13}H_{11}N_3O_2S_2$: C, 51.13; H, 3.63, N, 13.75. Found: C, 51.27; H, 3.46; N, 13.70.
52	A	54	IR ν_{max} (Nujol)/cm^{-1} 2925, 2855, 1625, 1506, 1461, 1411, 1370 and 763; NMR δ_H (400 MHz, $CDCl_3$) 2.99 (3H, s), 7.23 (1H, dd, *J* 5.0, 4.0 Hz), 7.53 (1H, d, *J* 5.5 Hz), 7.82 (1H, dd, *J* 5.0, 1.5 Hz), 8.14 (1H, d, *J* 5.0 Hz) and 8.62 (1H, dd, *J* 4.0, 1.5 Hz); Anal. Calcd for $C_{12}H_8N_2OS_2$: C, 55.36; H, 3.10; N, 10.76. Found: C, 55.45; H, 3.13; N, 10.74.
53	D	48	mp 144 - 146 °C; IR ν_{max} (Nujol)/cm^{-1} 2925, 2855, 1559, 1523, 1463, 1379, 1349, 764 and 715; NMR δ_H (400 MHz, $CDCl_3$) 2.76 (3H, s), 6.23 (1H, d, *J* 3.5 Hz), 7.00 (1H, dd, *J* 5.0, 3.5 Hz), 7.14 (1H, dt, *J* 3.5, 1.0 Hz), 7.21 (1H, d, *J* 3.5 Hz), 7.48 (1H, dd, *J* 5.0, 1.0 Hz), 7.58 (1H, d *J* 5.5 Hz) and 8.40 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{12}H_{10}N_2OS_2$: C, 54.94; H, 3.84; N, 10.68. Found: C, 54.76; H, 3.94; N, 10.67.

54	F	72	mp 199.9 – 200.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3385, 3043, 2925, 2854, 1679, 1642, 1571, 1546, 1521, 1459 and 1366; NMR δ_H (400 MHz, $CDCl_3$) 1.42 (9H, s), 3.49 – 3.51 (2H, m), 3.74 – 3.78 (2H, m), 4.90 – 5.04 (1H, s), 5.53 – 5.68 (1H, s), 7.21 – 7.25 (2H, m), 7.81 (1H, d, *J* 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.49 (1H, d, *J* 5.0 Hz); Anal. Calcd for $C_{18}H_{20}N_4O_3S_2$: C, 53.45; H, 4.98, N, 13.84. Found: C, 53.48; H, 4.98; N, 13.76.
55	G	77	mp >190 °C dec. ; IR ν_{max} (Nujol)/cm^{-1} 3186, 3103, 3066, 2922, 2854, 2422, 1624, 1462, 1407, 1377, 1347 and 1320; NMR δ_H (400 MHz, DMSO-d_6) 3.18 – 3.24 (2H, m), 3.72 – 3.84 (2H, m), 7.41 – 7.45 (2H, m), 7.65 – 7.88 (1H, s), 8.08 – 8.26 (2H, s), 8.32 (1H, d, *J* 4.0 Hz), 8.53 (1H, d, *J* 5.5 Hz) and 8.59 – 8.78 (1H, s); Anal. Calcd for $C_{13}H_{12}N_4O_2S_2 \cdot 0.5\ H_2O \cdot 2.1$ HCl: C, 40.04; H, 3.90, N, 14.37; Cl, 19.09. Found: C, 39.62; H, 3.87; N, 14.04; Cl, 19.20.
56	H	42	mp 188-191 °C; IR ν_{max} (Nujol)/cm^{-1} 3060, 1592, 1533, 1492, 1465, 1409, 1378, 1321, 1172, 1136, 1085, 919 and 737; NMR δ_H (400 MHz, $CDCl_3$) 3.20 (6H, s), 6.15 (1H, br s) 7.70 (1H, d, *J* 5.5 Hz), 8.33 (1H, d, *J* 5.5 Hz), 8.33 (0.5H, br s) and 9.05 (0.5H, br s); Anal. Calcd for $C_{14}H_{10}F_3N_3OS_2$: C, 47.05; H, 2.82; N, 11.75. Found: C, 46.69; H, 2.85; N, 11.20; M/Z 358 $(M+H)^+$.
57	A	44	mp 178-179 °C; NMR δ_H (400 MHz, $CDCl_3$) 7.70 (1H, d, *J* 1.4 Hz), 7.80 (1H, d, *J* 5.5 Hz), 8.43 (1H, d, *J* 5.6 Hz) and 8.57 (1H, d, *J* 1.4 Hz); Anal. Calcd for $C_{12}H_4F_3BrN_2OS_2$; C, 36.66; H, 1.03; N, 7.12. Found C, 36.76; H, 1.21; N, 7.09.
58	F	50	mp 200.4 – 200.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3275, 3115, 2924, 2855, 1630, 1598, 1558, 1504, 1464 and 1363; NMR δ_H (400 MHz, $CDCl_3$) 3.23 (3H, d, *J* 5.0 Hz), 5.26 – 5.30 (1H, m), 7.22 – 7.27 (2H, m), 7.82 (1H, d, *J* 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.53 (1H, d, *J* 5.0 Hz); Anal. Calcd for $C_{14}H_{13}N_3OS_2 \cdot 0.3\ H_2O$: C, 54.45; H, 4.44; N, 13.61. Found: C, 54.77; H, 4.65; N, 13.35.
59	F	38	mp 142.1 – 142.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3265,3125, 3074, 2925,2855, 1634, 1593, 1561, 1461, 1408 and 1365; NMR δ_H (400 MHz, $CDCl_3$) 4.29 – 4.34 (2H, m), 5.21 (1H, d, *J* 9.1 Hz), 5.34 – 5.38 (2H, m), 6.06 – 6.14 (1H, m), 7.23 – 7.27 (2H, m), 7.83 (1H, d, *J* 5.0 Hz), 8.04 (1H, d, *J* 5.5 Hz) and 8.52 (1H, d, *J* 5.0 Hz); Anal. Calcd for $C_{14}H_{11}N_3OS_2$: C, 55.79; H, 3.68, N, 13.94. Found: C, 55.59; H, 3.79; N, 13.64.
60	B	51	mp 185-187 °C; IR ν_{max} (Nujol)/cm^{-1} 3079, 2925, 2855, 2182, 1608, 1587, 1454 and 784; NMR δ_H (400 MHz, $CDCl_3$) 1.08 (3H, t, *J* 7.5 Hz), 1.95 (2H, m), 2.82 (2H, t, *J* 7.5 Hz), 7.02 (1H, ddd, *J* 9.0, 5.0, 1.0 Hz), 7.31 (1H, d, *J* 5.5 Hz), 7.64 (1H, dt, *J* 8.0, 1.0 Hz), 7.73 (1H, ddd, *J* 9.0, 8.0, 2.0 Hz), 7.78 (1H, d, *J* 5.5 Hz) and 8.38 (1H, d, *J* 5.0 Hz); Anal. Calcd for $C_{16}H_{14}N_4S$: C, 65.28; H, 4.79; N, 19.03. Found: C, 65.09; H, 4.72; N, 18.84.
61	F	20	mp 134.8 – 135.6 °C; IR ν_{max} (Nujol)/cm^{-1} 3380,3087, 2956, 2925, 2854, 1623, 1572, 1519, 1408 and 1365; NMR δ_H (400 MHz, $CDCl_3$) 1.35 (6H, d, *J* 6.5 Hz), 4.36 – 4.45 (1H, m), 5.11 (1H, d, *J* 7.4 Hz), 7.21 – 7.25 (2H, m), 7.81 (1H, d, *J* 6.0 Hz), 8.00 (1H, d, *J* 5.5 Hz) and 8.50 (1H, d, *J* 4.0 Hz).

62	A	5	mp 262 – 263 °C; NMR δ_H (400 MHz, $CDCl_3$) 3.30 (3H, s), 7.49 (2H, t, *J* 12.0 Hz), 7.56 (2H, t, *J* 12.0 Hz), 7.70 (1H, d, *J* 5.5 Hz), 8.2 - 8.0 (2H, m) and 8.41 (1H, d, *J* 5.5Hz); Anal. Calcd for $C_{17}H_9F_3N_2OS_2$; C, 53.96; H, 2.40; N, 7.40. Found C, 53.86; H, 2.33; N, 7.27.
63	A	13	mp 122-125 °C; IR ν_{max} (Nujol)/cm^{-1} 2956, 2925, 2855, 1633, 1551, 1505, 1464, 1409, 1378, 1236, 762 and 729; NMR δ_H (400 MHz, $CDCl_3$) 1.07 (3H, t, *J* 7.5 Hz), 2.06 (2H, m), 3.22 (2H, t, *J* 7.5 Hz), 7.24 (1H, dd, *J* 5.0, 4.0 Hz), 7.50 (1H, d, *J* 5.5 Hz), 7.83 (1H, dd, *J* 5.0, 1.0 Hz), 8.14 (1H, d, *J* 5.5 Hz) and 8.60 (1H, dd, *J* 4.0, 1.0 Hz); Anal. Calcd for $C_{14}H_{12}N_2OS_2$: C, 58.31; H, 4.20; N, 9.71. Found: C, 58.53; H, 4.24; N, 9.69.
64	B	62	mp 266-269 °C; IR ν_{max} (Nujol)/cm^{-1} 3078, 2925, 2855, 2180, 1613, 1590, 1503, 1454 and 783; NMR δ_H (400 MHz, $CDCl_3$) 2.60 (3H, s), 7.02 (1H, m), 7.29 (1H, d, *J* 5.0 Hz), 7.63 (1H, d, *J* 8.5 Hz), 7.73 (1H, m), 7.78 (1H, d, *J* 5.0 Hz) and 8.39 (1H, d, *J* 5.0 Hz); Anal. Calcd for $C_{14}H_{10}N_4S$: C, 63.14; H, 3.80; N, 21.04. Found: C, 63.21; H, 3.78; N, 21.13.
65	F	19	mp 135.6 – 135.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3300 – 3100, 3094, 3080, 2925, 2854, 1635, 1578, 1367, 1239 and 763; NMR δ_H (400 MHz, $CDCl_3$) 3.43 (3H, s), 3.69 (2H, t, *J* 5.3 Hz), 3.84 (2H, q, *J* 5.4 Hz), 5.60 (1H, t, *J* 5.6 Hz), 7.21 – 7.25 (2H, m), 7.81 (1H, d, *J* 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.50 (1H, d, *J* 5.0 Hz); Anal. Calcd for $C_{14}H_{13}N_3O_2S_2.0.4\ H_2O$: C, 51.48; H, 4.26; N, 12.87. Found: C, 51.77; H, 4.60; N, 12.48.
66	F	24	mp >150 °C dec.; NMR δ_H (400 MHz, DMSO-d_6) 2.92 (3H, s), 2.93 (3H, s), 3.41 – 3.48 (2H, m), 3.92 – 3.40 (2H, m), 7.43 – 7.46 (2H, m), 7.78 – 7.96 (1H, s), 8.33 (1H, d, *J* 5.0 Hz), 8.54 (1H, d, *J* 5.5 Hz) 8.65 – 8.70 (1H, s) and 10.01 – 10.27 (1H, br s).
67	D	99	IR ν_{max} (Nujol)/cm^{-1} 3069, 2928, 2855, 1533, 1462, 1369 and 696; NMR δ_H (400 MHz, $CDCl_3$) 0.96 (3H, t, *J* 7.5 Hz), 1.84 (2H, m), 2.94 (2H, t, *J* 7.5 Hz), 6.19 (1H, dd, *J* 4.0, 1.0 Hz), 6.96 (1H, dd, *J* 5.0, 3.5 Hz), 7.08 (1H, dt, *J* 3.5, 1.0 Hz), 7.18 (1H, d, *J* 4.0 Hz), 7.43 (1H, dd, *J* 5.0, 1.0 Hz), 7.54 (1H, d *J* 5.5 Hz) and 8.42 (1H, d, *J* 5.5 Hz).
68	I	71	mp 160-162 °C; IR ν_{max} (Nujol)/cm^{-1} 3076, 1620, 1543, 1529, 1463, 1414, 1402, 1342, 1202, 1174, 1139, 1049, 817, 801, 770, 757 and 570; NMR δ_H (400 MHz, $CDCl_3$) 4.08 (3H, s), 6.25 (1H, d, *J* 4.5 Hz), 7.60 (1H, d, *J* 5.6 Hz), 8.36 (1H, d, *J* 5.6 Hz) and 8.68 (1H, br s); Anal. Calcd for $C_{13}H_7F_3N_2O_2S_2$: C, 45.35; H, 2.05; N, 8.13. Found: C, 45.34; H, 2.10; N, 8.15.
69	A	26	IR ν_{max} (Nujol)/cm^{-1} 3065, 2923, 2854, 1624, 1533, 1465, 1409, 1377, 1257, 1059 and 728; NMR δ_H (400 MHz, $CDCl_3$) 7.29 (1H, dd, *J* 4.0, 5.0 Hz), 7.92 (1H, dd, *J* 1.0, 5.0 Hz), 8.27 (1H, s) and 8.73 (1H, dd, *J* 1.0. 4.0 Hz).
70	F	84	IR ν_{max} (Nujol)/cm^{-1} 3093, 2923, 2854, 1629, 1573, 1499, 1463, 1404, 1371, 1248, 1193, 1056 and 732; NMR δ_H (400 MHz, $CDCl_3$) 3.43 (6H, s), 7.29 (1H, dd, *J* 4.0, 5.0 Hz), 7.82 (1H, dd, *J* 1.0, 5.0 Hz), 7.96 (1H, s) and 8.48 (1H, dd, *J* 1.0. 4.0 Hz).

71	J	87	IR ν_{max} (Nujol)/cm^{-1} 2295, 2854, 1624, 1567, 1534, 1462, 1409, 1368, 1250, 1194, 1049 and 763; NMR δ_H (400 MHz, $CDCl_3$) 3.41 (6H, s), 7.24 (1H, dd, *J* 4.0, 5.0 Hz), 7.37 (1H, tt, *J* 1.0, 7.5 Hz), 7.45-7.50 (2H, m), 7.82 (1H, dd, *J* 1.0, 5.0 Hz), 8.05-8.09 (2H, m), 8.11 (1H, s) and 8.50 (1H, dd, *J* 1.0. 4.0 Hz).
72	F	32	mp 114.1 – 114.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3300 – 3210, 3102, 2925, 2855, 1656, 1581, 1552, 1461, 1339 and 1229; NMR δ_H (400 MHz, $CDCl_3$) 2.97 – 3.29 (1H, s), 3.68 – 3.72 (2H, m), 3.87 – 3.90 (2H, m), 5.63 (1H, t, *J* 5.2 Hz), 7.28 (1H, d, *J* 5.5 Hz), 7.49 – 7.54 (2H, m), 7.61 – 7.67 (1H, m), 8.02 (1H, d, *J* 5.5 Hz) and 8.26 – 8.30 (2H, m).
73	F	24	mp 164.6 – 165.4 °C; IR ν_{max} (Nujol)/cm^{-1} 3064, 2925, 2855, 1632, 1558, 1410, 1375, 1339, 1235 and 1049; NMR δ_H (400 MHz, $CDCl_3$) 1.56 (3H, t, *J* 6.8 Hz), 4.67 (2H, q, *J* 7.1 Hz), 7.24 – 7.26 (1H, m), 7.42 (1H, d, *J* 5.5 Hz), 7.84 (1H, d, *J* 4.0 Hz), 8.16 (1H, d, *J* 5.5 Hz) and 8.58 (1H, d, *J* 4.0 Hz); Anal. Calcd for $C_{13}H_{10}N_2O_2S_2$: C, 53.78; H, 3.47, N, 9.64. Found: C, 53.55; H, 3.51; N, 9.57.
74	A	8	mp 185 - 186 °C; IR ν_{max} (Nujol)/cm^{-1} 3082, 2955, 1630, 1626, 1504, 1306, 1219, 1202, 1178, 1166, 1144, 1132, 922, 806 and 775; NMR δ_H (400 MHz, $CDCl_3$) 2.12 (3H, s), 2.43 (3H, s), 7.80 (1H, d, *J* 5.5 Hz) and 8.30 – 8.45 (2H, m).
75	F	99	mp 146.5 – 148.1 °C; IR ν_{max} (Nujol)/cm^{-1} 4329, 4259, 2920, 2669, 1621, 1562, 1463 and 1377; NMR δ_H (400 MHz, DMSO) 2.85 (3H, s), 2.86 (3H, s), 3.36 (3H, s), 3.42 (1H, q, *J* 6.2 Hz), 4.19 (1H, t, *J* 6.0 Hz), 7.38 – 7.40 (2H, m), 8.26 (1H, d, *J* 3.5 Hz), 8.46 (1H, d, *J* 3.0 Hz) and 8.49 (1H, d, *J* 5.5 Hz).
76	F	26	mp 143.3 – 143.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3262, 3119, 2924, 2854, 1729, 1628, 1594, 1557 and 1367; NMR δ_H (400 MHz, $CDCl_3$) 1.25 (3H, t, *J* 7.2 Hz), 2.09 (2H, quin, *J* 7.1 Hz), 2.49 (2H, t, *J* 7.3 Hz), 3.72 (2H, q, *J* 6.5 Hz), 4.14 (2H, q, *J* 7.2 Hz), 5.35 – 5.43 (1H, m), 7.22 – 7.28 (2H, m), 7.83 (1H, d, *J* 5.0 Hz), 8.03 (1H, d, *J* 5.5 Hz) anf 8.51 (1H, d, *J* 4.0 Hz). Anal. Calcd for $C_{17}H_{17}N_3O_3S_2$: C, 54.38; H, 4.56; N, 11.19. Found: C, 54.28; H, 4.53; N, 11.02.
77	F	91	mp 199.9 – 200.5 °C; IR ν_{max} (Nujol)/cm^{-1} 3079, 3064, 2923, 2854, 1620, 1562, 1497, 1465, 1415, 1376, 1264 and 765; NMR δ_H (400 MHz, $CDCl_3$) 3.88 (4H, t, *J* 4.7 Hz), 4.0 (4H, t, *J* 5.0 Hz), 7.22 – 7.28 (2H, m), 7.82 (1H, d, *J* 5.0 Hz), 8.02 (1H, d, *J* 6.0 Hz), 8.43 (1H, dd, *J* 3.7, 1.4 Hz). Anal. Calcd for $C_{15}H_{13}N_3O_2S_2$: C, 54.36; H, 3.95; N, 12.67. Found: C, 54.40; H, 3.88; N, 12.52.
78	F	60	mp >120 °C dec; IR ν_{max} (Nujol)/cm^{-1} 3309, 3251, 3107, 3066, 2924, 2854, 1623, 1588, 1556, 1502, 1461, 1408, 1367 and 1234; NMR δ_H (400 MHz, DMSO) 3.11 – 3.23 (2H, m), 3.41 – 3.49 (2H, m), 3.55 – 3.65 (2H, m), 3.75 – 4.04 (7H, m), 7.35 – 7.41 (2H, m), 7.78 – 7.86 (1H, s), 8.26 (1H, d, *J* 4.0 Hz), 8.48 (1H, d, *J* 5.5 Hz), 8.54 – 8.69 (1H, s) and 10.41 – 10.71 (1H, s).

79	K	87	IR ν_{max} (Nujol)/cm^{-1} 2925, 2855, 1632, 1568, 1535, 1504, 1458, 1410, 1370, 1249, 1193, 1056, 762, and 723; NMR δ_H (400 MHz, $CDCl_3$) 3.42 (6H, s), 6.53 (1H, dd, *J* 1.5, 3.0 Hz), 7.22 (1H, dd, *J* 4.0, 5.0 Hz), 7.38 (1H, d, *J* 3.0 Hz), 7.47 - 7.49 (1H, m), 7.80 (1H, dd, *J* 1.5, 5.0 Hz), 8.16 (1H, s) and 8.47 (1H, dd, *J* 1.5, 4.0 Hz).
80	K	61	IR ν_{max} (Nujol)/cm^{-1} 2925, 2855, 1630, 1571, 1461, 1408, 1378, 1249, 1220, 1192, 1045, and 760; NMR δ_H (400 MHz, $CDCl_3$) 3.44 (6H, s), 7.13 (1H, dd, *J* 3.5, 5.0 Hz), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.35 (1H, dd, *J* 1.0, 5.0 Hz), 7.81 (1H, dd, *J* 1.5, 5.0 Hz), 7.82 (1H, dd, *J* 1.0, 3.5 Hz), 8.10 (1H, s) and 8.48 (1H, dd, *J* 1.5, 4.0 Hz).
81	F	67	mp 214.6-215.3 °C; NMR δ_H (400 MHz, DMSO) 4.41 (2H, s), 7.33 – 7.38 (2H, m), 8.24 (1H, d, *J* 5.1 Hz), 8.44 (1H, d, *J* 5.6 Hz), 8.59 (1H, s) and 8.72 – 8.75 (1H, m). Anal. Calcd for $C_{11}H_8N_4OS_2$: C, 47.81; H, 2.92; N, 20.27. Found: C, 48.03; H, 2.96; N, 20.05.
82	F	93	IR ν_{max} (Nujol)/cm^{-1} 3301, 1637, 1565, 1527, 1506, 1412, 1308, 1249, 1219, 1195, 1066, 1045 and 1026; NMR δ_H (400 MHz, $CDCl_3$) 3.46 (3H, s), 4.00 (4H, s), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.27 (1H, m), 7.81 (1H, dd, *J* 1.0, 5.0 Hz), 8.00 (1H, d, *J* 5.5 Hz) and 8.45 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.10 min (9:1).
83	F	93	IR ν_{max} (Nujol)/cm^{-1} 1627, 1562, 1529, 1504, 1412, 1300, 1267, 1248, 1196, 1147, 1096 and 1007; NMR δ_H (400 MHz, $CDCl_3$) 2.41 (3H, s), 2.62 (4H, t, *J* 5.0Hz), 4.08 (4H, t, *J* 5.0Hz), 7.24 (1H, dd, *J* 4.0, 5.0 Hz), 7.26 (1H, d, *J* 5.5 Hz), 7.81 (1H, dd, *J* 1.0, 5.0 Hz), 8.00 (1H, d, *J* 5.5 Hz) and 8.42 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.77 min (9:1), detection wavelength λ 210 nm.
84	F	94	IR ν_{max} (Nujol)/cm^{-1} 1675, 1626, 1565, 1527, 1497, 1411, 1263, 1169, 1134, 1048 and 989; NMR δ_H (400 MHz, $CDCl_3$) 1.52 (9H, s), 3.61 (4H, t, *J* 5.3 Hz), 4.02 (4H, t, *J* 5.0 Hz), 7.25 (1H, dd, *J* 4.0, 5.0 Hz), 7.27 (1H, d, *J* 5.5 Hz), 7.83 (1H, dd, *J* 1.0, 5.0 Hz), 8.03 (1H, d, *J* 5.5 Hz) and 8.41 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 2.89 min (10:0).
85	F	92	IR ν_{max} (Nujol)/cm^{-1} 3347, 1634, 1562, 1506, 1412, 1340, 1322, 1241, 1224 and 1078; NMR δ_H (400 MHz, $CDCl_3$) 1.88 (1H, m), 2.01 – 2.16 (2H, m), 2.23 (1H, m), 3.79 – 4.02 (4H, m), 4.47 (1H, m), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.26 (1H, d, *J* 5.5 Hz), 7.82 (1H, dd, *J* 1.0, 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.48 (1H, dd, *J* 1.5, 4.0 Hz); Retention time: 3.48 min (9:1).
86	F	90	IR ν_{max} (Nujol)/cm^{-1} 3284, 1630, 1566, 1500, 1408, 1299, 1268, 1247, 1222, 1190 and 1052; NMR δ_H (400 MHz, $CDCl_3$) 1.67 (2H, m), 2.06 (2H, m), 3.53 (2H, m), 4.05 (4H, septet, *J* 4.0 Hz), 4.60 (1H, m), 4.64 (1H, m), 7.24 (1H, dd, *J* 4.0, 5.0 Hz), 7.26 (1H, d, *J* 5.5 Hz), 7.81 (1H, dd, *J* 1.5, 5.0 Hz), 8.00 (1H, d, *J* 5.5 Hz) and 8.42 (1H, dd, *J* 1.5, 4.0 Hz); Retention time: 3.36 min (9:1).

87	F	84	IR ν_{max} (Nujol)/cm^{-1} 3385, 2727, 2475, 1629, 1609, 1563, 1499, 1453, 1409, 1278, 1231, 1163 and 1046; NMR δ_H (400 MHz, DMSO) 3.25 (4H, m), 4.16 (4H, m), 7.36 (1H, dd, *J* 4.0, 5.0 Hz), 7.39 (1H, d, *J* 5.5 Hz), 8.21 (1H, dd, *J* 1.0, 5.0 Hz), 8.37 (1H, dd, *J* 1.0, 4.0 Hz), 8.50 (1H, d, *J* 5.5 Hz) and 9.50 (2H, br s); Retention time: 3.27 min (8:2).
88	A	18	mp 194 - 195 °C; IR ν_{max} (Nujol)/cm^{-1} 3076, 1626, 1534, 1521, 1457, 1400, 1354, 1268, 1042, 1012 909, 786, 779 and 767; NMR δ_H (400 MHz, $CDCl_3$) 6.72 (1H, m) 7.59 (1H, d, *J* 5.6 Hz), 7.86 (1H, d, *J* 1.3 Hz), 8.30 (1H, d, *J* 5.6 Hz) and 8.51 (1H, d, *J* 1.3 Hz),; Anal. Calcd for $C_{11}H_4Cl_2N_2OS_2$: C, 49.92; H, 1.90; N, 10.58. Found: C, 50.06; H, 1.96; N, 10.50.
89	F	43	IR ν_{max} (Nujol)/cm^{-1} 3281, 1635, 1581, 1526, 1504, 1411, 1323, 1241, 1199, 1078 and 1049; NMR δ_H (400 MHz, $CDCl_3$) 1.38 (3H, d, *J* 6.5 Hz), 2.70 (1H, br s), 3.76 (1H, dd, *J* 5.9 and 11.1 Hz), 3.89 (1H, dd, *J* 4.1 and 11.1 Hz), 4.47 (1H, m), 5.68 (1H, br s), 7.24 (1H, dd, *J* 4.0, 5.0 Hz), 7.25 (1H, d, *J* 5.5 Hz), 7.82 (1H, dd, *J* 1.0, 5.0 Hz), 8.03 (1H, d, *J* 5.5 Hz) and 8.48 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.61 min (8:2).
90	F	70	mp 212.2-212.5 °C; IR ν_{max} (Nujol)/cm^{-1} 3288, 3082, 2924, 2854, 1636, 1568, 1533, and 1355; NMR δ_H (400 MHz, DMSO) 1.84 (3H, s), 3.28-3.39 (2H, m), 3.49-3.61 (2H, m), 7.32 (1H, d, *J* 5.5 Hz), 7.37 (1H, t, *J* 4.5 Hz), 7.52-7.61 (1H, m), 7.97 – 8.04 (1H, m), 8.24 (1H, d, *J* 4.5 Hz), 8.42 (1H, d, *J* 5.5 Hz) and 8.50 – 8.72 (1H, s). Anal. Calcd for $C_{15}H_{14}N_4O_2S_2$: C, 52.01; H, 4.07; N, 16.17. Found: C, 52.02; H, 4.09; N, 16.03.
91	A	19	mp 160 - 161 °C; IR ν_{max} (Nujol)/cm^{-1} 3091, 1661, 1582, 1531, 1519, 1463, 1415, 1357, 1255, 1214, 1014, 931, 827, 762, 698 and 685; NMR δ_H (400 MHz, $CDCl_3$) 7.55 (1H, m), 7.65 (1H, d, *J* 5.6 Hz), 8.35 (1H, d, *J* 5.5 Hz), 8.75 (1H, m), 8.90 (1H, m) and 9.65 (1H, b s); Anal. Calcd for $C_{11}H_5ClN_2O_2S$: C, 52.28; H, 2.19; N, 15.23. Found: C, 52.25; H, 2.22; N, 15.08.
92	F	31	IR ν_{max} (Nujol)/cm^{-1} 3406, 1631, 1564, 1501, 1410, 1279, 1246, 1224, 1192 and 1054; NMR δ_H (400 MHz, DMSO) 1.16 (6H, d, *J* 6.1 Hz), 2.70 (2H, m), 2.89 (2H, m), 4.75 (2H, m), 6.50 (1H, s), 7.36 – 7.42 (2H, m), 8.27 (1H, dd, *J* 1.0, 5.0 Hz), 8.37 (1H, dd, *J* 1.0, 4.0 Hz) and 8.48 (1H, d, *J* 5.5 Hz); Retention time: 3.60 min (8:2).
93	F	39	IR ν_{max} (Nujol)/cm^{-1} 3401, 1633, 1569, 1525, 1500, 1407, 1243, 1198 and 1052; NMR δ_H (400 MHz, $CDCl_3$) 3.44 – 3.62 (6H, m), 3.77 (1H, m), 7.29 (2H, m), 7.33 (1H, dd, *J* 4.0, 5.0 Hz), 8.21 (1H, dd, *J* 1.0, 5.0 Hz), 8.38 (1H, d, *J* 5.5 Hz) and 8.64 (1H, br s); Retention time: 2.87 min (8:2).

94	F	66	IR ν_{max} (Nujol)/cm^{-1} 3278, 1621, 1588, 1557, 1521, 1497, 1409, 1326, 1245, 1223, 1199, 1077 and 1049; NMR δ_H (400 MHz, $CDCl_3$) 1.73 (1H, m), 1.95 (2H, m), 2.07 (1H, m), 3.67 (1H, m), 3.82 (1H, m), 3.88 (1H, m), 3.96 (1H, m), 4.23 (1H, m), 5.71 (1H, br s), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.25 (1H, d, *J* 5.5 Hz), 7.81 (1H, dd, *J* 1.0, 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.50 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 4.97 min (8:2).
95	F	24	mp 178.6-179.3 °C; IR ν_{max} (Nujol)/cm^{-1} 3261, 2924, 2854, 1629, 1590, 1556, 1409, and 1367; NMR δ_H (400 MHz, DMSO) 4.82 (2H, d, *J* 5.5 Hz), 7.27 (2H, app t, *J* 3.0 Hz), 7.34 (1H, d, *J* 5.5 Hz), 7.74 (1H, t, *J* 8.8 Hz), 8.11 – 8.23 (2H, m), 8.43 (1H, d, *J* 5.6 Hz), and 8.56 (1H, d, *J* 4.1 Hz). Anal. Calcd for $C_{17}H_{12}N_4OS_2 \cdot 0.25\ H_2O$: C, 57.20; H, 3.53; N, 15.70. Found: C, 57.03; H, 3.37; N, 15.60.
96	F	22	mp >140°C dec; IR ν_{max} (Nujol)/cm^{-1} 3261, 3104, 2925, 2854, 1630, 1591, 1555, and 1365; NMR δ_H (400 MHz, DMSO) 4.71 (2H, d, *J* 5.4 Hz), 6.31 (1H, 1H, d, *J* 3.1 Hz), 6.38 – 6.41 (1H, m), 7.34 – 7.37 (2H, m), 7.60 – 7.61 (1H, m), 8.04 (1H, t, *J* 5.9 Hz), 8.23 (1H, d, *J* 5.1 Hz), and 8.55 – 8.71 (1H, s). Anal. Calcd for $C_{16}H_{11}N_3O_2S_2 \cdot 0.5\ H_2O$: C, 54.84; H, 3.45; N, 11.99. Found: C, 54.62; H, 3.31; N, 11.89.
97	A	14	mp 186 - 188 °C; IR ν_{max} (Nujol)/cm^{-1} 3074, 3071, 1622, 1541, 1529, 1503, 1463, 1411, 1373, 1247, 1215, 1085, 1025, 932, 822, and 760; NMR δ_H (400 MHz, $CDCl_3$) 7.13 (1H, d, *J* 4.4 Hz), 7.61 (1H, d, *J* 5.9 Hz), 8.30 (1H, d, *J* 5.9 Hz), and 8.40 (1H, d, *J* 4.4 Hz); Anal. Calcd for $C_{12}H_6ClN_3OS$: C, 41.92; H, 1.28; N, 8.88. Found: C, 42.14; H, 1.35; N, 8.79.
98	F	94	IR ν_{max} (Nujol)/cm^{-1} 3345, 1634, 1562, 1506, 1411, 1224 and 1078; NMR δ_H (400 MHz, $CDCl_3$) 1.87 (1H, m), 2.00 – 2.16 (2H, m), 2.23 (1H, m), 3.79 – 4.02 (4H, m), 4.45 (4H, m), 7.23 (1H, d, *J* 5.5 Hz), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.82 (1H, dd, *J* 1.5, 5.0 Hz), 8.01 (1H, d, *J* 5.5 Hz) and 8.49 (1H, dd, *J* 1.5, 4.0 Hz); Retention time: 3.43 min (9:1)..
99	F	29	IR ν_{max} (Nujol)/cm^{-1} 3259, 1599, 1558, 1522, 1498, 1409, 1335, 1235, 1197, 1116 and 1050; NMR δ_H (400 MHz, $CDCl_3$) 1.91 (2H, quintet, *J* 6.5 Hz), 2.51 (4H, m), 2.57 (2H, t, *J* 6.6 Hz), 3.71 (2H, q, *J* 6.0 Hz), 3.78 (4H, t, *J* 4.5 Hz), 6.24 (1H, br s), 7.22 (2H, m), 7.80 (1H, dd, *J* 1.0, 5.0 Hz), 8.00 (1H, d, *J* 5.5 Hz) and 8.51 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 2.84 min (9:1).
100	F	64	IR ν_{max} (Nujol)/cm^{-1} 3292, 1634, 1576, 1523, 1502, 1408, 1315, 1242, 1198 and 1050; NMR δ_H (400 MHz, $CDCl_3$) 1.92 (2H, quintet, *J* 6.1 Hz), 3.75 – 3.82 (4H, m), 5.54 (1H, m), 7.22 (1H, dd, *J* 4.0, 5.0 Hz), 7.24 (1H, d, *J* 5.5 Hz), 7.81 (1H, dd, *J* 1.5, 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.50 (1H, dd, *J* 1.5, 4.0 Hz); Retention time: 2.62 min (9:1).

101	F	91	IR ν_{max} (Nujol)/cm^{-1} 3340, 1634, 1576, 1521, 1502, 1411, 1323, 1246, 1201, 1052 and 1041; NMR δ_H (400 MHz, $CDCl_3$) 1.38 (3H, d, *J* 6.5 Hz), 2.86 (1H, br s), 3.76 (1H, m), 3.88 (1H, m), 4.43 (1H, m), 5.32 (1H, d, *J* 6.9 Hz), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.23 (1H, d, *J* 5.5 Hz), 7.82 (1H, dd, *J* 1.5, 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.49 (1H, dd, *J* 1.5, 4.0 Hz); Retention time: 3.62 min (8:2).
102	F	72	IR ν_{max} (Nujol)/cm^{-1} 3339, 1633, 1575, 1521, 1500, 1411, 1323, 1246, 1201, 1052 and 1041; NMR δ_H (400 MHz, $CDCl_3$) 1.38 (3H, d, *J* 6.6 Hz), 2.87 (1H, br s), 3.75 (1H, m), 3.89 (1H, m), 4.43 (1H, m), 5.33 (1H, d, *J* 7.3 Hz), 7.23 (1H, d, *J* 5.5 Hz), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.81 (1H, dd, *J* 1.0, 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.49 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.63 min (8:2).
103	F	76	IR ν_{max} (Nujol)/cm^{-1} 3400, 3235, 1633, 1573, 1527, 1501, 1408, 1356, 1234, 1199, 1129, 1080 and 1051; NMR δ_H (400 MHz, $CDCl_3$) 1.33 (3H, d, *J* 7.0 Hz), 2.99 (1H, br s), 3.52 (1H, ddd, *J* 5.5, 7.5, 14.0 Hz), 3.80 (1H, ddd, *J* 3.0, 6.5, 14.0 Hz), 4.18 (1H, m), 5.68 (1H, t, *J* 6.0 Hz), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.24 (1H, d, *J* 5.5 Hz), 7.81 (1H, dd, *J* 1.0, 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.49 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.72 min (8:2).
104	F	51	IR ν_{max} (Nujol)/cm^{-1} 3258, 3101, 1628, 1593, 1557, 1524, 1504, 1408, 1331, 1240, 1228, 1200, 1089 and 1046; NMR δ_H (400 MHz, $CDCl_3$) 2.25 (2H, quintet, *J* 6.8 Hz), 3.68 (2H, q, *J* 6.7 Hz), 4.14 (2H, t, *J* 6.8 Hz), 5.29 (1H, t, *J* 6.0 Hz), 6.98 (1H, m), 7.09 (1H, m), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.25 (1H, d, *J* 5.5 Hz), 7.55 (1H, s), 7.83 (1H, dd, *J* 1.0, 5.0 Hz), 8.04 (1H, d, *J* 5.5 Hz) and 8.49 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.69 min (8:2).
105	F	3	mp 210 – 212 °C; IR ν_{max} (Nujol)/cm^{-1} 3241, 3084, 3046, 1654, 1596, 1571, 1521, 1459, 1365, 1353, 1201, 1060 1042, 978, 804, 763, and 705; NMR δ_H (400 MHz, $CDCl_3$) 6.65 (1H, m), 7.23 (1H, m), 7.75 (1H, m), 7.97 (1H, d, *J* 3.5 Hz) and 8.31 (1H, d, *J* 3.5 Hz); Anal. Calcd for $C_{13}H_{11}N_3O_2S$: C, 57.13; H, 4.06; N, 15.37. Found: C, 57.01; H, 4.02; N, 15.24.
106	F	11	mp 161 - 163 °C; IR ν_{max} (Nujol)/cm^{-1} 3099, 1636, 1562, 1533, 1518, 1463, 1409, 1396, 1354, 1264, 1214, 1050, 1019, 882, 793, and 668; NMR δ_H (400 MHz, $CDCl_3$) 3.72 (2H, m), 3.85 (2H, m), 5.64 (1H, b m), 7.31 (1H, d, J 5.6 Hz), 7.49 (1H, m), 8.00 (1H, m), 8.56 (1H, m), 8.83 (1H, b s) and 9.60 (1H, b s); Anal. Calcd for $C_{14}H_{12}N_4O_2S$: C, 55.99; H, 4.03; N, 18.65. Found: C, 56.00; H, 4.02; N, 18.80.
107	F	32	IR ν_{max} (Nujol)/cm^{-1} 3258, 3106, 1634, 1592, 1555, 1516, 1407, 1356, 1317, 1252, 1160, 1129, 1047 and 1017; NMR δ_H (400 MHz, $CDCl_3$) 3.85 (3H, s), 3.88 (3H, s), 4.79 (2H, d, *J* 5.1 Hz), 5.53 (1H, t, *J* 6.0 Hz), 6.85 (1H, m), 6.99 (2H, m), 7.19 (1H, dd, *J* 4.0, 5.0 Hz), 7.26 (1H, d, *J* 5.5 Hz), 7.77 (1H, dd, *J* 1.0, 5.0 Hz), 8.03 (1H, d, *J* 5.5 Hz) and 8.44 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 5.17 min (8:2).

108	F	59	IR ν_{max} (Nujol)/cm^{-1} 3063, 1633, 1567, 1519, 1500, 1410, 1302, 1281, 1245, 1193, 1112 and 1014; NMR δ_H (400 MHz, $CDCl_3$) 3.38 (6H, s), 3.72 (4H, t, *J* 6.0 Hz), 4.06 (4H, t, *J* 6.0Hz), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.24 (1H, d, *J* 5.5 Hz), 7.80 (1H, dd, *J* 1.0, 5.0 Hz), 7.98 (1H, d, *J* 5.5 Hz) and 8.47 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 5.85 min (8:2).
109	F	94	mp 229.1-229.4°C; IR ν_{max} (Nujol)/cm^{-1} 3091, 3050, 2924, 2834, 1625, 1570, 1523, 1460, 1407 and 1376; NMR δ_H (400 MHz, DMSO) 2.03 – 2.09 (4H, m), 3.60 – 3.81 (4H, m),7.35 – 7.40 (2H, m), 8.25 (1H, d, *J* 5.0 Hz), 8.43 (1H, d, *J* 5.5 Hz), and 8.49 (1H, dd, *J* 5.0, 1.1 Hz). Anal. Calcd for $C_{15}H_{13}N_3OS_2$: C, 57.12; H, 4.15; N, 13.32. Found: C, 57.16; H, 4.11; N, 13.12.
110	R	99	IR ν_{max} (Nujol)/cm^{-1} 3476, 3298, 3160, 1631, 1562, 1536, 1455, 1406, 1239, 1080 and 1050; NMR δ_H (400 MHz, $CDCl_3$), 5.19 (2H, s), 7.24 (1H, dd, *J* 4.0, 5.0 Hz), 7.27 (1H, d, *J* 5.5 Hz), 7.82 (1H, dd, *J* 1.0, 5.0 Hz), 8.06 (1H, d, *J* 5.5 Hz) and 8.55 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.59 min (8:2).
112	F	85	IR ν_{max} (Nujol)/cm^{-1} 3374, 1623, 1567, 1522, 1409, 1250, 1223, 1188, 1062 and 1050; NMR δ_H (400 MHz, DMSO) 2.00 (1H, m), 2.11 (1H, m), 3.55 – 3.90 (4H, m), 4.47 (1H, m), 5.06 (1H, m), 7.35 (1H, m), 7.36 (1H, d, *J* 5.5 Hz), 8.24 (1H, br d, *J* 5.0 Hz), 8.41 (1H, d, *J* 5.5 Hz) and 8.46 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 4.48 min (8:2).
113	F	90	IR ν_{max} (Nujol)/cm^{-1} 3301, 1618, 1565, 1520, 1409, 1250, 1222, 1188, 1105 and 1049; NMR δ_H (400 MHz, DMSO) 1.99 (1H, m), 2.10 (1H, m), 3.66 – 3.81 (4H, m), 4.47 (1H, m), 5.06 (1H, m), 7.35 (1H, dd, *J* 4.0, 5.0 Hz), 7.36 (1H, d, *J* 5.5 Hz), 8.23 (1H, br d, *J* 5.0 Hz), 8.41 (1H, d, *J* 5.5 Hz) and 8.46 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 4.50 min (8:2).
114	F	56	IR ν_{max} (Nujol)/cm^{-1} 3554, 3287, 1626, 1585, 1526, 1501, 1410, 1311, 1243, 1200, 1074 and 1047; NMR δ_H (400 MHz, DMSO) 3.62 (4H, m), 4.15 (1H, br s), 4.71 (2H, t, *J* 5.5 Hz), 7.04 (1H, br s), 7.29 (1H, d, *J* 5.5 Hz), 7.35 (1H, dd, *J* 4.0, 5.0 Hz), 8.22 (1H, dd, *J* 1.0, 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.74 (1H, br s); Retention time: 2.84 min (8:2).
115	F	10	mp 155.9-156.3°C; IR ν_{max} (Nujol)/cm^{-1} 3104, 2925, 2854, 1733, 1565, 1513, 1463, 1408 and 1372; NMR δ_H (400 MHz, $CDCl_3$)1.58 (3H, s), 2.07 – 2.33 (3H, m), 2.36 – 2.51 (1H, m), 3.60 – 4.20 (4H, m), 7.16 – 7.45 (2H, m), 7.82 (1H, d, *J* 3.9 Hz), 8.01 (1H, s), and 8.50 (1H, s). Anal. Calcd for $C_{17}H_{15}N_3O_3S_2 \cdot 0.5\ H_2O$: C, 53.39; H, 4.22; N, 10.99. Found: C, 53.54; H, 4.08; N, 10.57
116	A	52	IR ν_{max} (Nujol)/cm^{-1} 3092, 2924, 2854, 1613, 1502, 1462, 1404, 1376 and 1253; NMR δ_H (400 MHz, $CDCl_3$) 2.78 (3H, s), 7.08 (1H, d, *J* 5.1 Hz), 7.59 (1H, d, *J* 6.1 Hz), 7.76 (1H, d, 5.1 Hz), and 8.31 (1H, d, *J* 5.6 Hz).
117	F	80	mp 165.1–165.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3066, 2924, 2854, 1626, 1569, 1508, 1462, 1399 and 1366; NMR δ_H (400 MHz, $CDCl_3$) 2.76 (3H, s), 3.38 (6H, s), 7.03 (1H, d, *J* 4.5 Hz), 7.24 – 7.27 (1H, m), 7.64 (1H, d, *J* 4.5 Hz), and 7.96 (1H, d, *J* 5.5 Hz). Anal. Calcd for $C_{14}H_{13}N_3OS_2 \cdot 0.1\ H_2O$: C, 55.09; H, 4.36; N, 13.77. Found: C, 54.97; H, 4.27; N, 13.59

118	F	42	mp 194.5-195.0 °C; IR ν_{max} (Nujol)/cm^{-1} 3337, 3265, 3117, 2924, 2854, 1592, 1462 and 1399; NMR δ_H (400 MHz, DMSO) 2.68 (3H, s), 3.55 – 3.62 (2H, m), 3.63 – 3.69 (2H, m), 4.74 (1H, t, *J* 5.1 Hz), 7.21 (1H, d, *J* 5.0 Hz), 7.26 – 7.34 (2H, m), 8.08 (1H, d, *J* 5.1 Hz), and 8.41 (1H, d, *J* 5.6 Hz).Anal. Calcd for $C_{14}H_{13}N_3O_2S_2$: C, 52.65; H, 4.10; N, 13.15. Found: C, 52.40; H, 4.08; N, 13.01
119	F	22	mp 126.4-127.1 °C; IR ν_{max} (Nujol)/cm^{-1} 3537, 3499, 3438, 3082, 2955, 2854, 1613, 1568, 1533, 1506, 1409 and 1375; NMR δ_H (400 MHz, $CDCl_3$) 1.48 (6H, s), 3.81 (2H, d, *J* 2.9 Hz), 5.40 (1H, s), 5.80 – 5.90 (1H, s), 7.20 – 7.29 (2H, m), 7.82 (1H, d, *J* 5.0 Hz), 8.03 (1H, d, *J* 5.5 Hz), 8.48 (1H, d, *J* 4.0 Hz).Anal. Calcd for $C_{15}H_{15}N_3O_2S_2$: C, 54.04; H, 4.53; N, 12.60. Found: C, 54.21; H, 4.65; N, 12.17
120	F	22	mp 151.6-152.4 °C; NMR δ_H (400 MHz, DMSO) 3.16 – 3.25 (2H, m), 3.39 (3H, s), 4.01 – 4.12 (2H, m), 7.36 – 7.42 (2H, m), 8.02 – 8.14 (2H, s), 8.25 (1H, d, *J* 5.0 Hz), 8.45 – 8.47 (1H, m) and 8.49 (1H, d, *J* 6.1 Hz). Anal. Calcd for $C_{14}H_{14}N_4OS_2 \cdot 2HCl \cdot 1.5\ H_2O$: C, 40.19; H, 4.58; N, 13.39. Found: C, 39.78; H, 4.35; N, 13.39
121	F	37	mp >131 °C dec; NMR δ_H (400 MHz, $CDCl_3$) 2.12 –2.28 (3H, m), 2.62 – 2.72 (1H, m), 3.81 – 3.93 (1H, m), 3.96 – 4.05 (1H, m), 4.71 – 4.79 (1H, m), 7.21 (1H, t, *J* 4.5 Hz), 7.30 (1H, d, 5.6 Hz), 7.78 – 7.82 (1H, m), 8.10 (1H, d, *J* 5.5 Hz), and 8.46 – 8.49 (1H, m). Anal. Calcd for $C_{16}H_{13}N_3O_3S_2 \cdot 0.5\ H_2O$: C, 52.16; H, 3.83; N, 11.41. Found: C, 52.27; H, 3.70; N, 11.51
122	A	50	mp 185.7 – 186.2 °C; IR ν_{max} (Nujol)/cm^{-1} 3074, 2924, 2854, 1739, 1623, 1461, 1409, 1376 and 1203; NMR δ_H (400 MHz, $CDCl_3$) 1.57 (3H, t, *J* 7.1 Hz), 4.66 (2H, q, *J* 7.1 Hz), 7.30 (1H, t, *J* 5.0 Hz), 7.85 (1H, d, *J* 5.4 Hz), 7.89 – 7.92 (1H, m), 8.34 (1H, d, *J* 5.5 Hz), and 8.88 (1H, d, *J* 4.1 Hz); Anal. Calcd for $C_{14}H_{10}N_2O_3S_2$: C, 52.82; H, 3.17; N, 8.79. Found: C, 52.53; H, 3.14; N, 8.70
123	F	46	mp 144.6-145.2 °C; IR ν_{max} (Nujol)/cm^{-1} 3380, 3266, 3113, 3076, 2925, 2855, 1739, 1596, 1564, 1365 and 1207; NMR δ_H (400 MHz, $CDCl_3$) 3.81 (3H, s), 4.45 (2H, d, *J* 5.7 Hz), 5.78 (1H, t, *J* 5.6 Hz), 7.22 – 7.29 (1H, m), 7.83 (1H, d, *J* 3.5 Hz), 8.06 (1H, d, *J* 5.6 Hz) and 8.49- 8.51 (1H, m). Anal. Calcd for $C_{14}H_{11}N_3O_3S_2$: C, 50.44; H, 3.33; N, 12.60. Found: C, 50.44; H, 3.32; N, 12.55
124	L	50	mp >250 °C dec; IR ν_{max} (Nujol)/cm^{-1} 3084, 3078, 2924, 2854, 2730, 2647, 1723, 1621, 1459, 1410, 1377 and 1233; NMR δ_H (400 MHz, DMSO) 7.43 (1H, t, *J* 4.5 Hz), 7.91 (1H, d, *J* 5.5 Hz), 8.32 (1H, d, *J* 5.1 Hz), 8.82 (1H, d, *J* 5.6 Hz), 8.87 (1H, d, *J* 3.0 Hz) and 13.70 – 13.90 (1H, s). Anal. Calcd for $C_{12}H_{16}N_2O_3S_2 \cdot 0.75\ H_2O$: C, 47.44; H, 2.49; N, 9.22. Found: C, 47.39; H, 2.73; N, 9.23
125	F	67	mp 232.1 – 233.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3443, 3378, 3178, 2924, 2854, 1737, 1644, 1562, 1510, 1498, 1462, 1406, 1358 and 1321; NMR δ_H (400 MHz, DMSO) 3.98 – 4.09 (2H, m), 7.03 – 7.09 (1H, s), 7.31 – 7.39 (2H, m), 7.42 – 7.48 (1H, s), 7.56 – 7.66 (1H, m), 8.24 (1H, d, *J* 4.4 Hz), 8.44 (1H, d, *J* 5.5 Hz) and 8.55 – 8.75 (1H, s).

126	M	74	mp 232.8 – 233.0 °C; IR ν_{max} (Nujol)/cm^{-1} 3101, 3087, 3073, 2924, 2854, 1728, 1620, 1463, 1410, 1248 and 758; NMR δ_H (400 MHz, DMSO) 4.06 (3H, s), 7.43 (1H, t, *J* 4.5 Hz), 7.93 (1H, d, *J* 5.5 Hz), 8.32 (1H, d, *J* 4.4 Hz) and 8.79 – 8.86 (2H, m). Anal. Calcd for $C_{13}H_8N_2O_3S_2$: C, 51.31; H, 2.65; N, 9.20. Found: C, 51.31; H, 2.65; N, 9.09
127	L	70	mp 232.9 – 234.0 °C; IR ν_{max} (Nujol)/cm^{-1} 3289, 2925, 2854, 2429, 1712, 1630, 1565, 1409 and 1371; NMR δ_H (400 MHz, DMSO) 3.96 – 4.38 (2H, m), 7.28 – 7.44 (2H, m), 7.68 – 7.93 (1H, s), 8.25 (1H, s, *J* 4.5 Hz), 8.44 (1H, d, *J* 5.0 Hz), 8.57 – 8.82 (1H, s) and 12.01 – 13.19 (1H, s). Anal. Calcd for $C_{13}H_{19}N_3O_3S_2 \cdot 0.5\ H_2O$: C, 47.55; H, 3.07; N, 12.80. Found: C, 47.46; H, 2.84; N, 12.87
128	N	65	mp 242.1 – 242.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3262, 3202, 3102, 3018, 2955, 2924, 2854, 1622, 1574, 1547, 1409, 1362, 1340, 1234 and 1160; NMR δ_H (400 MHz, DMSO) 3.06 (3H, s), 7.38 (1H, t, *J* 4.2 Hz), 7.47 (1H, d, *J* 5.5 Hz), 8.28 (1H, d, *J* 3.5 Hz), 8.54 (1H, d, *J* 5.5 Hz), 9.47 (1H, s) and 9.74 (1H, s); Anal. Calcd for $C_{12}H_{10}N_4O_3S_3$: C, 40.67; H, 2.84; N, 15.80. Found: C, 40.99; H, 2.92; N, 15.53
129	F	99	mp 96.2 – 96.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3339, 3080, 3061, 2924, 2854, 1630, 1561, 1503, 1458, 1401, 1371 ,1079 and 773; NMR δ_H (400 MHz, $CDCl_3$) 1.81 – 1.92 (1H, m), 1.97 – 2.30 (3H, m), 2.79 (3H, s), 3.78- 3.95 (3H, m), 3.98 – 4.08 (1H, m), 4.42 – 4.53 (1H, s), 7.07 (1H, d, *J* 5.0 Hz), 7.25 (1H, d, *J* 5.6 Hz), 7.68 (1H, d, *J* 5.0 Hz) and 8.03 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{17}H_{17}N_3O_2S_2$: C, 55.96; H, 4.86; N, 11.52. Found: C, 55.92; H, 4.78; N, 11.14
130	O	44	mp 258.3 – 259.0 °C; IR ν_{max} (Nujol)/cm^{-1} 3276, 2928, 2854, 1667, 1629, 1584, 1556, 1463, 1407 and 1365; NMR δ_H (400 MHz, DMSO) 2.02 (3H, s), 7.38 (1H, t, *J* 4.5 Hz), 7.42 (1H, d, *J* 5.5 Hz), 8.28 (1H, d, *J* 3.6 Hz), 8.51 (1H, d, *J* 5.5 Hz), 8.67 – 8.72 (1H, s), 9.30 (1H, s) and 10.02 (1H, s); Anal. Calcd for $C_{13}H_{10}N_4O_2S_2 \cdot 0.5\ H_2O$: C, 47.69; H, 3.39; N, 17.11. Found: C, 47.52; H, 3.04; N, 16.87
131	P	68	mp 252.8– 253.3 °C; IR ν_{max} (Nujol)/cm^{-1} 3308, 3243, 3073, 2924, 2854, 1642, 1586, 1557, 1463, 1407, 1364, 1326 and 762; NMR δ_H (400 MHz, DMSO) 3.69 (2H, t, *J* 5.5 Hz), 4.98 (1H, d, *J* 10.4 Hz), 5.14 (1H, d, *J* 17.1 Hz), 5.74 – 5.86 (1H, m), 6.67 – 6.82 (1H, s), 7.35 (1H, t, *J* 4.2 Hz), 7.43 (1H, d, *J* 5.6 Hz), 8.09 (1H, s), 8.25 (1H, d, *J* 4.5 Hz), 8.51 (1H, d, *J* 5.5 Hz), 8.79 (1H, s) and 9.17 (1H, s); Anal. Calcd for $C_{15}H_{13}N_5O_2S_2 \cdot 0.25\ H_2O$: C, 49.50; H, 3.74; N, 19.24. Found: C, 49.38; H, 3.64; N, 19.11
132	F	44	mp 138.1 – 138.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3258, 3108, 3047, 2926, 2855, 1593, 1553, 1519, 1505, 1463, 1391, 1372, 1229 and 776; NMR δ_H (400 MHz, $CDCl_3$) 2.24 (2H, quin, *J* 6.9 Hz), 2.76 (3H, s), 3.69 (2H, q, *J* 6.5 Hz), 4.13 (2H, t, *J* 7.1 Hz), 5.27 – 5.29 (1H, m), 6.96 (1H, s), 7.04 (1H, d, *J* 5.0 Hz), 7.08 (1H, s), 7.24 (1H, t, *J* 5.6 Hz), 7.53 (1H, s), 7.67 (1H, d, *J* 5.1 Hz) and 8.04 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{18}H_{17}N_5OS_2 \cdot 0.3\ H_2O$: C, 55.59; H, 4.56; N, 18.01. Found: C, 55.56; H, 4.40; N, 17.85

133	F	26	IR ν_{max} (Nujol)/cm^{-1} 3400, 3232, 1633, 1573, 1528, 1501, 1408, 1356, 1234, 1199, 1129, 1080 and 1051; NMR δ_H (400 MHz, $CDCl_3$) 1.33 (3H, d, *J* 6.5 Hz), 2.95 (1H, br s), 3.53 (1H, ddd, *J* 5.5, 7.5, 14.0 Hz), 3.81 (1H, ddd, *J* 3.0, 6.5, 14.0 Hz), 4.18 (1H, m), 5.67 (1H, t, *J* 6.0 Hz), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.25 (1H, d, *J* 5.5 Hz), 7.81 (1H, dd, *J* 1.0, 5.0 Hz), 8.03 (1H, d, *J* 5.5 Hz) and 8.50 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.74 min (8:2).
134	Q	65	mp 143.6 – 144.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3319, 3107, 3098, 3061, 2924, 2854, 2764, 1663, 1624, 1353, 1460, 1400, 1376 and 764; NMR δ_H (400 MHz, $CDCl_3$) 2.28 (6H, s), 2.55 (2H, t, *J* 6.5 Hz), 3.55 (2H, q, *J* 6.2 Hz), 7.44 (1H, t, *J* 4.3 Hz), 7.90 (1H, d, *J* 5.5 Hz), 8.33 (1H, d, *J* 5.1 Hz) and 8.76 – 8.84 (3H, m); Anal. Calcd for $C_{16}H_{16}N_4O_2S_2 \cdot 0.55\ H_2O$: C, 51.89; H, 4.65; N, 15.13. Found: C, 51.54; H, 4.27; N, 15.02
135	F	14	Byproduct from the preparation of Example 143. IR ν_{max} (Nujol)/cm^{-1} 3145, 3088, 1725, 1620, 1546, 1509, 1435, 1410, 1339, 1234 and 1064; NMR δ_H (400 MHz, $CDCl_3$) 2.26 (2H, quintet, *J* 7.5 Hz), 2.79 (2H, t, *J* 8.0 Hz), 4.32 (2H, t, *J* 7.0Hz), 7.32 (1H, dd, *J* 4.0, 5.0 Hz), 7.57 (1H, d, *J* 5.5 Hz), 7.85 (1H, dd, *J* 1.0, 5.0 Hz), 8.21 (1H, d, *J* 5.5 Hz) and 9.23 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.58 min (8:2).
136	Q	71	mp 173.1 – 174.0 °C; IR ν_{max} (Nujol)/cm^{-1} 3082, 2924, 2854, 1654, 1630, 1541, 1500, 1459, 1406, 1374, 1137 and 756; NMR δ_H (400 MHz, DMSO) 2.96 (3H, s), 3.15 (3H, s), 7.40 (1H, t, *J* 4.2 Hz), 7.82 (1H, d, *J* 5.6 Hz), 8.28 (1H, d, *J* 5.0 Hz), 8.58 – 8.61 (1H, m) and 8.80 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{14}H_{11}N_3O_2S_2$: C, 52.98; H, 3.49; N, 13.23. Found: C, 53.02; H, 3.44; N, 13.23
137	S	60	IR ν_{max} (Nujol)/cm^{-1} 3106, 1717, 1625, 1528, 1503, 1409, 1340, 1273, 1232 and 1045; NMR δ_H (400 MHz, $CDCl_3$) 2.40 (6H, s), 7.26 (1H, m), 7.67 (1H, d, *J* 5.5 Hz), 7.86 (1H, dd, *J* 1.0, 5.0 Hz), 8.34 (1H, d, *J* 5.5 Hz) and 8.57 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 2.70 min (8:2).
138	T	58	IR ν_{max} (Nujol)/cm^{-1} 3195, 3121, 1678, 1622, 1539, 1499, 1411, 1342, 1254, 1227, 1211, 1062 and 1021; NMR δ_H (400 MHz, $CDCl_3$) 2.57 (3H, s), 7.29 (1H, dd, *J* 4.0, 5.0 Hz), 7.49 (1H, d, *J* 5.5 Hz), 7.86 (1H, dd, *J* 1.0, 5.0 Hz), 8.22 (1H, d, *J* 5.5 Hz), 8.24 (1H, br s) and 8.89 (1H, br s); Retention time: 3.22 min (8:2).
139	F	18	IR ν_{max} (Nujol)/cm^{-1} 3424, 3091, 1629, 1555, 1502, 1409, 1326, 1238, 1101, 1055 and 1003; NMR δ_H (400 MHz, $CDCl_3$) 7.28 (1H, m), 7.31 (1H, dd, *J* 4.0, 5.0 Hz), 7.61, (1H, d, *J* 5.5 Hz), 7.93 (1H, dd, *J* 1.5, 5.0 Hz), 8.14 (1H, t, *J* 1.5 Hz), 8.33 (1H, d, *J* 5.5 Hz), 8.53 (1H, dd, *J* 1.5, 4.0 Hz) and 8.88 (1H, m); Retention time: 5.52 min (8:2).
140	F	76	IR ν_{max} (Nujol)/cm^{-1} 3252, 3072, 1595, 1557, 1524, 1497, 1405, 1305, 1279, 1240, 1197, 1087 and 1046; NMR δ_H (400 MHz, $CDCl_3$) 2.22 (2H, quintet, *J* 6.8 Hz), 3.65 (1H, q, *J* 6.5 Hz), 4.08 (2H, t, *J* 6.8 Hz), 5.21 (1H, t, *J* 6.0 Hz), 6.18 (2H, t, *J* 2.0 Hz), 6.71 (2H, t, *J* 2.0 Hz), 7.23 (1H, m), 7.24 (1H, d, *J* 5.5 Hz), 7.81 (1H, dd, *J* 1.0, 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.47 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 7.36 min (8:2).

141	F	88	IR ν_{max} (Nujol)/cm^{-1} 3096, 1628, 1617, 1518, 1409, 1359, 1255, 1226, 1212, 1174 and 1050; NMR δ_H (400 MHz, $CDCl_3$) 4.12 (3H, s), 7.21 (1H, dd, *J* 4.0, 5.0 Hz), 7.49 (1H, d, *J* 5.5 Hz), 7.82 (1H, dd, *J* 1.0, 5.0 Hz), 8.14 (1H, dd, *J* 1.0, 4.0 Hz) and 8.29 (1H, d, *J* 5.5 Hz); m/z 361 MH^+; Retention time: 3.10 min (8:2).
142	F	15	IR ν_{max} (Nujol)/cm^{-1} 3257, 3120, 1630, 1559, 1497, 1408, 1237, 1089 and 1046; NMR δ_H (400 MHz, $CDCl_3$) 2.98 (2H, t, *J* 7.0 Hz), 3.57 (3H, s), 3.91 (2H, q, *J* 6.8 Hz), 5.46 (1H, t, *J* 6.0 Hz), 6.05 (1H, m), 6.10 (1H, t, *J* 3.0 Hz), 6.59 (1H, t, *J* 2.5 Hz), 7.21 (1H, dd, *J* 4.0, 5.0 Hz), 7.24 (1H, d, *J* 5.5 Hz), 7.79 (1H, dd, *J* 1.0, 5.0 Hz), 8.02 (1H, d, *J* 5.5 Hz) and 8.49 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 7.51 min (8:2).
143	F	13	IR ν_{max} (Nujol)/cm^{-1} 3298, 1694, 1633, 1567, 1503 and 1082; NMR δ_H (400 MHz, DMSO) 1.88 (2H, t, *J* 7.0 Hz), 2.36 (2H, t, *J* 7.0 Hz), 3.48 (2H, m), 7.30 (1H, m), 7.35 (1H, br d, *J* 4.0 Hz), 7.62 (1H, m), 8.23 (1H, br d, *J* 5.0 Hz), 8.39 (1H, br d, *J* 5.5 Hz) and 8.57 (1H, br s); Retention time: 5.31 min (8:2).
144	F	52	IR ν_{max} (Nujol)/cm^{-1} 3230, 3093, 1635, 1563, 1523, 1504, 1408, 1229, 1080 and 1046; NMR δ_H (400 MHz, $CDCl_3$) 1.43 (1H, br s), 3.06 (2H, t, *J* 6.5 Hz), 3.96 (2H, q, *J* 6.2 Hz), 5.70 (1H, m), 6.90 (1H, s), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.26 (1H, m), 7.81 (1H, dd, *J* 1.0, 5.0 Hz), 8.01 (1H, d, *J* 5.5 Hz) and 8.50 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.87 min (8:2), detection wavelength λ 210 nm.
145	F	71	IR ν_{max} (Nujol)/cm^{-1} 3102, 1629, 1597, 1536, 1516, 1500, 1407, 1260, 1215, 1169 and 1051; NMR δ_H (400 MHz, DMSO) 6.79 (2H, m), 7.27 (1H, dd, *J* 4.0, 5.0 Hz), 7.40 (2H, m), 7.63 (1H, d, *J* 5.5 Hz), 8.08 (1H, dd, *J* 1.5, 4.0 Hz), 8.19 (1H, dd, *J* 1.5, 5.0 Hz), 8.74 (1H, d, *J* 5.5 Hz) and 10.11 (1H, s); m/z 437 MH^-; Retention time: 4.29 min (8:2).
146	F	27	NMR δ_H (400 MHz, $CDCl_3$) 2.41 (3H, br s), 4.05 (2H, m), 4.69 (2H, t, *J* 6.1 Hz), 5.48 (1H, t, *J* 6.0 Hz), 7.24 (1H, m), 7.25 (1H, d, *J* 5.5 Hz), 7.83 (1H, dd, *J* 1.5, 5.0 Hz), 7.94 (1H, s), 8.08 (1H, d, *J* 5.5 Hz) and 8.46 (1H, dd, *J* 1.5, 4.0 Hz); Retention time: 3.55 min (8:2).
147	F	39	IR ν_{max} (Nujol)/cm^{-1} 3098, 3057, 1632, 1535, 1510, 1411, 1264, 1203, 1167 and 1050; NMR δ_H (400 MHz, DMSO) 3.64 (3H, s), 7.26 (1H, dd, *J* 4.0, 5.0 Hz), 7.65 (1H, d, *J* 5.5 Hz), 8.01 (1H, dd, *J* 1.5, 4.0 Hz), 8.17 (1H, dd, *J* 1.5, 5.0 Hz), 8.73 (1H, d, *J* 5.5 Hz) and 8.96 (1H, s); Retention time: 2.59 min (8:2).
148	F	52	IR ν_{max} (Nujol)/cm^{-1} 3070, 1635, 1536, 1521, 1408, 1223, 1200, 1098 and 1050; NMR δ_H (400 MHz, DMSO) 2.84 (3H, s), 7.30 (1H, t, *J* 4.5 Hz), 7.70 (1H, d, *J* 5.5 Hz), 8.24 (2H, m) and 8.77 (1H, d, *J* 5.5 Hz); m/z 377 MH^+; Retention time: 5.48 min (8:2).
149	F	38	IR ν_{max} (Nujol)/cm^{-1} 3109, 3072, 2446, 2389, 1625, 1529, 1516, 1412, 1300, 1255, 1213, 1170 and 1076; NMR δ_H (400 MHz, DMSO) 3.85 (3H, s), 7.31 (1H, dd, *J* 4.0, 5.0 Hz), 7.67 (1H, d, *J* 5.5 Hz), 7.91 (1H, d, *J* 1.5 Hz), 8.07 (1H, d, *J* 1.5 Hz), 8.09 (1H, dd, *J* 1.5, 4.0 Hz), 8.20 (1H, dd, *J* 1.5, 5.0 Hz) and 8.78 (1H, d, *J* 5.5 Hz); Retention time: 2.97 min (8:2).

150	U	55	NMR δ_H (400 MHz, DMSO) 0.85 (6H, d, *J* 6.5 Hz), 1.96 (3H, m), 3.37 (2H, q, *J* 6.0 Hz), 3.54 (2H, m), 7.29 (1H, d, *J* 5.5 Hz), 7.35 (1H, dd, *J* 4.0, 5.0 Hz), 7.47 (1H, m), 7.90 (1H, m), 8.20 (1H, br d, *J* 4.0 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.59 (1H, br s); Retention time: 3.92 min (8:2).
151	U	50	NMR δ_H (400 MHz, DMSO) 1.11 –1.35 (5H, m), 1.58 – 1.69 (5H, m), 2.08 (1H, m), 3.35 (2H, q, *J* 6.0 Hz), 3.53 (2H, m), 7.30 (1H, d, *J* 5.5 Hz), 7.36 (1H, dd, *J* 4.0, 5.0 Hz), 7.48 (1H, m), 7.78 (1H, m), 8.21 (1H, br d, *J* 4.5 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.59 (1H, br s); Retention time: 4.81 min (8:2).
152	U	63	NMR δ_H (400 MHz, DMSO) 3.60 (2H, q, *J* 6.0 Hz), 3.67 (2H, m), 7.29 (1H, d, *J* 5.5 Hz), 7.34 (1H, dd, *J* 4.0, 5.0 Hz), 7.44 (2H, m), 7.51 (1H, m), 7.63 (1H, m), 7.85 (2H, m), 8.20 (1H, dd, *J* 1.0, 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.58 (2H, m); Retention time: 4.45 min (8:2).
153	U	63	NMR δ_H (400 MHz, DMSO) 3.59 (2H, q, *J* 6.0 Hz), 3.68 (2H, m), 7.29 (1H, d, *J* 5.5 Hz), 7.35 (1H, dd, *J* 4.0, 5.0 Hz), 7.52 (2H, m), 7.58 (1H, m), 7.87 (2H, m), 8.20 (1H, dd, *J* 1.0, 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.66 (2H, m); Retention time: 6.24 min (8:2).
154	U	44	NMR δ_H (400 MHz, DMSO) 3.56 (2H, q, *J* 6.0 Hz), 3.66 (2H, m), 7.14 (1H, dd, *J* 4.0, 5.0 Hz), 7.30 (1H, d, *J* 5.5 Hz), 7.35 (1H, dd, *J* 4.0, 5.0 Hz), 7.64 (1H, m), 7.74 (2H, m), 8.21 (1H, dd, *J* 1.0, 5.0 Hz), 8.40 (1H, d, *J* 5.5 Hz) and 8.60 (2H, m); Retention time: 4.30 min (8:2).
155	U	55	NMR δ_H (400 MHz, DMSO) 3.30 (2H, m), 3.50 (5H, m), 7.23 (1H, m), 7.29 (1H, d, *J* 5.5 Hz), 7.35 (1H, dd, *J* 4.0, 5.0 Hz), 7.56 (1H, m), 8.20 (1H, br d, *J* 5.0 Hz), 8.38 (1H, d, *J* 5.5 Hz) and 8.59 (1H, br s); Retention time: 3.45 min (8:2).
156	U	57	NMR δ_H (400 MHz, DMSO) 0.85 (6H, d, *J* 6.7 Hz), 1.82 (1H, m), 3.29 (2H, m), 3.55 (2H, m), 3.71 (2H, d, *J* 6.4 Hz), 7.20 (1H, m), 7.29 (1H, d, *J* 5.5 Hz), 7.35 (1H, dd, *J* 4.0, 5.0 Hz), 7.50 (1H, m), 8.20 (1H, br d, *J* 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.59 (1H, br s); Retention time: 4:80 min (8:2).
157	U	49	NMR δ_H (400 MHz, DMSO) 3.34 (2H, m), 3.57 (2H, m), 5.02 (2H, s), 7.30 – 7.36 (8H, m), 7.52 (1H, m), 8.20 (1H, br d, *J* 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.60 (1H, br s); Retention time: 5.01 min (8:2).
158	U	41	NMR δ_H (400 MHz, DMSO) 3.32 (2H, q, *J* 6.0 Hz), 3.56 (2H, m), 3.76 (2H, t, *J* 5.2 Hz), 4.20 (2H, t, *J* 5.2 Hz), 7.30 (1H, d, *J* 5.5 Hz), 7.36 (1H, dd, *J* 4.0, 5.0 Hz), 7.43 (1H, m), 7.52 (1H, m), 8.21 (1H, dd, *J* 1.0, 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.59 (1H, br s); Retention time: 3.90 min (8:2).
159	V	86	NMR δ_H (400 MHz, DMSO) 3.33 (2H, q, *J* 6.0 Hz), 3.52 (2H, m), 3.63 (2H, t, *J* 5.5 Hz), 4.99 (1H, dd, *J* 2.0, 10.2 Hz), 5.09 (1H, dd, *J* 2.0, 17.0 Hz), 5.79 (1H, m), 6.06 (2H, t, *J* 5.5 Hz), 7.30 (1H, d, *J* 5.5 Hz), 7.36 (1H, dd, *J* 4.0, 5.0 Hz), 7.53 (1H, m), 8.21 (1H, br d, *J* 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.60 (1H, br s); Retention time: 3.41 min (8:2).

160	V	84	NMR δ_H (400 MHz, DMSO) 1.03 – 1.25 (5H, m), 1.49 (1H, m), 1.61 (2H, m), 1.71 (2H, m), 3.32 (3H, m), 3.50 (2H, m), 5.79 (1H, d, *J* 7.9 Hz), 5.88 (1H, t, *J* 5.7 Hz), 7.30 (1H, d, *J* 5.5 Hz), 7.35 (1H, dd, *J* 4.0, 5.0 Hz), 7.53 (1H, m), 8.21 (1H, br d, *J* 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.59 (1H, br s); Retention time: 4.76 min (8:2).
161	V	89	NMR δ_H (400 MHz, DMSO) 3.35 (2H, q, *J* 6.1 Hz), 3.53 (2H, m), 4.20 (2H, d, J 5.9 Hz), 6.10 (1H, t, *J* 5.7 Hz), 6.42 (1H, t, *J* 6.0 Hz), 7.17 - 7.30 (6H, m), 7.34 (1H, dd, *J* 4.0, 5.0 Hz), 7.53 (1H, m), 8.19 (1H, br d, *J* 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz) and 8.59 (1H, br s); Retention time: 4.25 min (8:2).
162	V	99	NMR δ_H (400 MHz, DMSO) 3.43 (2H, q, *J* 5.9 Hz), 3.59 (2H, m), 6.30 (1H, t, *J* 5.7 Hz), 6.99 (1H, m), 7.19 – 7.46 (6H, m), 7.60 (1H, m), 8.20 (1H, br d, *J* 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz), 8.50 (1H, s) and 8.62 (1H, br s); Retention time: 5.12 min (8:2).
163	V	96	NMR δ_H (400 MHz, DMSO) 3.42 (2H, q, *J* 5.8 Hz), 3.59 (2H, m), 6.34 (1H, t, *J* 5.7 Hz), 7.23 – 7.40 (6H, m), 7.59 (1H, m), 8.20 (1H, br d, *J* 5.0 Hz), 8.39 (1H, d, *J* 5.5 Hz), 8.58 (1H, br s) and 8.66 (1H, s); Retention time: 7.72 min (8:2).
164	W	61	NMR δ_H (400 MHz, DMSO) 3.70 (2H, m), 3.83 (2H, m), 7.08 (1H, t, *J* 7.2 Hz), 7.24 – 7.37 (6H, m), 7.69 (1H, br s), 7.85 (1H, br s), 8.23 (1H, br d, *J* 5.0 Hz), 8.40 (1H, d, *J* 5.5 Hz), 8.62 (1H, br s) and 9.62 (1H, br s); Retention time: 4.47 min (8:2).
165	W	19	NMR δ_H (400 MHz, DMSO) 3.71 (2H, m), 3.82 (2H, m), 7.26 – 7.43 (6H, m), 7.63 (1H, m), 7.93 (1H, m), 8.22 (1H, br d, *J* 5.0 Hz), 8.40 (1H, d, *J* 5.5 Hz), 8.59 (1H, br s) and 9.63 (1H, br s); Retention time: 6.82 min (8:2).
166	W	41	NMR δ_H (400 MHz, DMSO) 1.09 – 1.22 (5H, m), 1.52 (1H, m), 1.62 (2H, m), 1.80 (2H, m), 3.63 (2H, m), 3.71 (2H, m), 3.94 (1H, m), 7.27 – 7.38 (4H, m), 7.59 (1H, m), 8.21 (1H, br d, *J* 5.0 Hz), 8.40 (1H, d, *J* 5.5 Hz) and 8.63 (1H, br s); Retention time: 5.98 min (8:2).
167	U	16	m/z 383 MH^+; Retention time: 2.96 min (8:2).
168	U	23	NMR δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.2 Hz), 1.40 (2H, sextet, *J* 7.6 Hz), 1.75 (2H, m), 3.02 (2H, m), 3.49 (2H, q, J 5.9 Hz), 3.84 (2H, q, *J* 5.7 Hz), 5.02 (1H, br s), 5.61 (1H, t, *J* 6.0 Hz), 7.23 (1H, dd, *J* 4.0, 5.0 Hz), 7.25 (1H, d, *J* 5.5 Hz), 7.82 (1H, d, *J* 1.0, 5.0 Hz), 8.04 (1H, d, *J* 5.5 Hz) and 8.48 (1H, dd, *J* 1.0, 4.0 Hz); Retention time: 3.91 min (8:2).
169	X	11	Mp 151 °C; NMR δ_H (400 MHz, DMSO) 2.92 (3H, s), 2.93 (3H, s), 4.46 (2H, br s), 7.39 (1H, dd, *J* 4.0, 5.0 Hz), 7.63 (1H, d, *J* 5.5 Hz), 8.28 (1H, dd, *J* 1.0, 5.0 Hz), 8.71 (1H, d, *J* 5.5 Hz), 9.31 (1H, br d, *J* 3.0 Hz), 10.05 (1H, br s) and 11.73 (1H, s); Retention time: 3.37 min (8:2).
170	Y	31	IR ν_{max} (Nujol)/cm^{-1} 3323, 1637, 1616, 1597, 1570, 1525, 1505, 1407, 1353, 1332, 1245, 1199, 1080 and 1051; NMR δ_H (400 MHz, DMSO) 3.33 (4H, q, *J* 6.0 Hz), 3.51 (4H, m), 6.15 (2H, t, *J* 5.9 Hz), 7.27 (2H, d, *J* 5.5 Hz), 7.31 (2H, dd, *J* 4.0, 5.0 Hz), 7.52 (2H, m), 8.17 (2H, dd, *J* 1.0, 5.0 Hz), 8.37 (2H, d, *J* 5.5 Hz) and 8.57 (2H, br s); m/z 635 MH^+.

Adenosine Receptor Binding

Binding Affinities at hA_{2A} Receptors

The compounds were examined in an assay measuring *in vitro* binding to human adenosine A_{2A} receptors expressed in HEK-293 cells by determining the displacement of the adenosine A_{2A} receptor selective radioligand [^{3}H]-CGS 21680 using standard techniques. The results are summarised in Table 3.

Table 3

Example	K_i (nM)
1	104
2	10
3	74
4	40
5	30
6	108
8	586
11	330
12	31
13	153
14	329
17	895
18	346
25	435
28	865
29	539
34	245
35	19
37	361
39	575
40	295
42	26
43	22
44	91

Example	K_i (nM)
45	26
46	101
47	46
48	151
49	18
50	33
51	8
52	32
54	36
55	78
56	309
57	800
58	15
59	18
60	237
61	21
63	37
64	529
65	21
66	218
67	469
68	105
72	126
73	48

Example	K_i (nM)
74	90
76	8
77	97
78	46
79	858
81	63
82	29
83	863
84	392
89	3
93	7
95	8
100	4
101	7
102	2
103	6
104	2
118	7
144	5
150	4
151	7
155	4
158	6
159	8

Evaluation of potential anti-Parkinsonian activity *in vivo*

Haloperidol-induced hypolocomotion model

It has previously been demonstrated that adenosine antagonists, such as theophylline, can reverse the behavioural depressant effects of dopamine antagonists, such as haloperidol, in rodents (Mandhane S.N. *et al.*, Adenosine A_2 receptors modulate haloperidol-induced catalepsy in rats. *Eur. J. Pharmacol.* 1997, **328**, 135 - 141). This approach is also considered a valid method for screening drugs with potential antiparkinsonian effects. Thus, the ability of novel adenosine antagonists to block haloperidol-induced deficits in locomotor activity in mice can be used to assess both *in vivo* and potential antiparkinsonian efficacy.

Method

Female TO mice (25-30g) obtained from TUCK, UK, are used for all experiments. Animals are housed in groups of 8 [cage size – 40 (width) x 40 (length) x 20 (height)cm] under 12hr light/dark cycle (lights on 08:00hr), in a temperature (20 ± 2°C) and humidity (55 ± 15%) controlled environment. Animals have free access to food and water, and are allowed at least 7 days to acclimatize after delivery before experimental use.

Drugs

Liquid injectable haloperidol (1 ml Serenance ampoules from Baker Norton, Harlow, Essex, each containing haloperidol BP 5 mg, batch # P424) are diluted to a final concentration of 0.02 mg/ml using saline. Test compounds are typically prepared as aqueous suspensions in 8% Tween. All compounds are administered intraperitoneally in a volume of 10 ml/kg.

Procedure

1.5 hours before testing, mice are administered 0.2 mg/kg haloperidol, a dose that reduces baseline locomotor activity by at least 50%. Test substances are typically administered 5-60 minutes prior to testing. The animals are then placed individually into clean, clear polycarbonate cages [20 (width) x 40 (length) x 20 (height) cm , with a flat perforated, Perspex lid]. Horizontal locomotor activity is determined by placing the cages within a frame containing a 3 x 6 array of photocells linked to a computer, which tabulates beam breaks. Mice are left undisturbed to explore for 1 hour, and the number of beams breaks

made during this period serves as a record of locomotor activity which is compared with data for control animals for statistically significant differences. In this model, Example 86, administered intraperitoneally at a dose of 10 mg/kg, significantly reversed haloperidol-induced hypolocomotion.

6-OHDA Model

Parkinson's disease is a progressive neurodegenerative disorder characterised by symptoms of muscle rigidity, tremor, paucity of movement (hypokinesia), and postural instability. It has been established for some time that the primary deficit in PD is a loss of dopaminergic neurones in the substantia nigra which project to the striatum, and indeed a substantial proportion of striatal dopamine is lost (ca 80-85%) before symptoms are observed. The loss of striatal dopamine results in abnormal activity of the basal ganglia, a series of nuclei which regulate smooth and well co-ordinated movement (Blandini F. *et al.*, Glutamate and Parkinson's Disease. *Mol. Neurobiol.* 1996, **12**, 73 - 94). The neurochemical deficits seen in Parkinson's disease can be reproduced by local injection of the dopaminergic neurotoxin 6-hydroxydopamine into brain regions containing either the cell bodies or axonal fibres of the nigrostriatal neurones.

By unilaterally lesioning the nigrostriatal pathway on only one-side of the brain, a behavioural asymmetry in movement inhibition is observed. Although unilaterally-lesioned animals are still mobile and capable of self maintenance, the remaining dopamine-sensitive neurones on the lesioned side become supersenstive to stimulation. This is demonstrated by the observation that following systemic administration of dopamine agonists, such as apomorphine, animals show a pronounced rotation in a direction contralateral to the side of lesioning. The ability of compounds to induce contralateral rotations in 6-OHDA lesioned rats has proven to be a sensitive model to predict drug efficacy in the treatment of Parkinson's Disease.

Animals

Male Sprague-Dawley rats, obtained from Charles River, are used for all experiments. Animals are housed in groups of 5 under 12hr light/dark cycle (lights on 08:00hr), in a temperature (20 ± 2°C) and humidity (55 ± 15%) controlled environment. Animals have free access to food and water, and are allowed at least 7 days to acclimatize after delivery before experimental use.

Drugs

Ascorbic acid, desipramine, 6-OHDA and apomorphine (Sigma-Aldrich, Poole, UK). 6-OHDA is freshly prepared as a solution in 0.2% ascorbate at a concentration of 4 mg/mL prior to surgery. Desipramine is dissolved in warm saline, and administered in a volume of 1 ml/kg. Apomorphine is dissolved in 0.02% ascorbate and administered in a volume of 2 mL/kg. Test compounds are suspended in 8%Tween and injected in a volume of 2 mL/kg.

Surgery

15 minutes prior to surgery, animals are given an intraperitoneal injection of the noradrenergic uptake inhibitor desipramine (25 mg/kg) to prevent damage to non-dopamine neurones. Animals are then placed in an anaesthetic chamber and anaesthetised using a mixture of oxygen and isoflurane. Once unconscious, the animals are transferred to a stereotaxic frame, where anaesthesia is maintained through a mask. The top of the animal's head is shaved and sterilised using an iodine solution. Once dry, a 2 cm long incision is made along the midline of the scalp and the skin retracted and clipped back to expose the skull. A small hole is then drilled through the skill above the injection site. In order to lesion the nigrostriatal pathway, the injection cannula is slowly lowered to position above the right medial forebrain bundle at –3.2 mm anterior posterior, -1.5 mm medial lateral from bregma, and to a depth of 7.2 mm below the duramater. 2 minutes after lowing the cannula, 2 µL of 6-OHDA is infused at a rate of 0.5 µL/min over 4 minutes, yeilding a final dose of 8 µg. The cannula is then left in place for a further 5 minutes to facilitate diffusion before being slowly withdrawn. The skin is then sutured shut using Ethicon W501 Mersilk, and the animal removed from the strereotaxic frame and returned to its homecage. The rats are allowed 2 weeks to recover from surgery before behavioural testing.

Apparatus

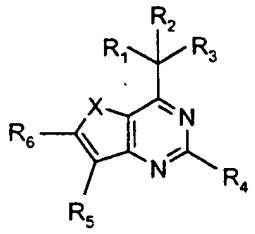
Rotational behaviour is measured using an eight station rotameter system provided by Med Associates, San Diego, USA. Each station is comprised of a stainless steel bowl (45 cm diameter x 15 cm high) enclosed in a transparent Plexiglas cover running around the edge of the bowl, and extending to a height of 29 cm. To assess rotation, rats are placed in cloth jacket attached to a spring tether connected to optical rotameter positioned above the bowl, which assesses movement to the left or right either as partial (45°) or full (360°) rotations. All eight stations are interfaced to a computer that tabulated data.

Procedure

To reduce stress during drug testing, rats are initially habituated to the apparatus for 15 minutes on four consecutive days. On the test day, rats are given an intraperitoneal injection of test compound 30 minutes prior to testing. Immediately prior to testing, animals are given a subcutaneous injection of a subthreshold dose of apomorphine, then placed in the harness and the number of rotations recorded for one hour. The total number of full contralatral rotations during the hour test period serves as an index of antiparkinsonian drug efficacy.

CLAIMS

1. A compound of formula (I):



(I)

wherein:

X is O or S;

R_1 and R_2 are independently selected from hydrogen, alkyl, aryl, hydroxy, alkoxy, aryloxy, cyano, nitro, CO_2R_7, COR_7, $OCOR_7$, $CONR_7R_8$, $CONR_7NR_8R_9$, $OCONR_7R_8$, NR_7R_8, NR_7COR_8, $NR_7CONR_8R_9$, $NR_7CO_2R_8$, $NR_7SO_2R_8$, $NR_7CONR_8NR_9R_{10}$, $NR_7NR_8CO_2R_9$, $NR_7NR_8CONR_9R_{10}$, $NR_7SO_2NR_8R_9$, SO_2R_7, SOR_7, SR_7 and $SO_2NR_7R_8$, or R_1 and R_2 together form a carbonyl group (C=O), an oxime group ($C=NOR_{11}$), an imine group ($C=NR_{11}$) or a hydrazone group ($C=NNR_{11}R_{12}$), or R_1 and R_2 together form a 5, 6 or 7 membered carbocyclic or heterocyclic ring;

R_3 is alkyl or aryl;

R_4, R_5 and R_6 are independently selected from hydrogen, alkyl, aryl, halogen, hydroxy, nitro, cyano, alkoxy, aryloxy, COR_7, $OCOR_7$, CO_2R_7, SR_7, SOR_7, SO_2R_7, $SO_2NR_7R_8$, $CONR_7R_8$, $CONR_7NR_8R_9$, $OCONR_7R_8$, NR_7R_8, NR_7COR_8, $NR_7CONR_8R_9$, $NR_7CO_2R_8$, $NR_7SO_2R_8$, $CR_7=NOR_8$, $NR_7CONR_8NR_9R_{10}$, $NR_7NR_8CO_2R_9$, $NR_7NR_8CONR_9R_{10}$, $SO_2NR_7NR_8R_9$, $NR_7SO_2NR_8R_9$, $NR_7NR_8SO_2R_9$, $NR_7NR_8COR_9$, $NR_7NR_8R_9$ and $NR_7CSNR_8R_9$, or R_5 and R_6 together form a 5, 6 or 7 membered carbocyclic or heterocyclic ring; and

R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are independently selected from hydrogen, alkyl and aryl,

or a pharmaceutically acceptable salt thereof or prodrug thereof.

2. A compound according to claim 1 wherein X is S.

3. A compound according to claim 1 or 2 wherein R_1 and R_2 are independently selected from hydrogen, hydroxy, cyano, alkyl and CO_2R_7.

4. A compound according to claim 3 wherein said alkyl group is a hydroxy-substituted alkyl.

5. A compound according to claim 3 wherein R_7 of said CO_2R_7 group is alkyl.

6. A compound according to claim 3, 4 or 5 wherein one of R_1 and R_2 is hydrogen.

7. A compound according to claim 3 wherein R_1 is hydrogen and R_2 is cyano.

8. A compound according to claim 1 or 2 wherein R_1 or R_2 together form a carbonyl group.

9. A compound according to claim 1 or 2 wherein R_1 and R_2 together form an oxime group, an imine group or a hydrazone group.

10. A compound according to any one of claims 1 to 9 wherein R_3 is aryl.

11. A compound according to any one of claims 1 to 10 wherein R_3 is selected from thienyl, furyl, pyrrolyl, thiazolyl, phenyl and pyridyl.

12. A compound according to claim 11 wherein R_3 is selected from 2-thienyl and 2-pyridyl.

13. A compound according to any preceding claim wherein R_5 is selected from hydrogen, alkyl and halogen.

14. A compound according to any preceding claim wherein R_6 is selected from hydrogen, alkyl, aryl and halogen.

15. A compound according to any of claims 1 to 12 wherein both R_5 and R_6 are hydrogen.

16. A compound according to any of claims 1 to 15 wherein R_4 is selected from alkyl, halogen, alkoxy, alkylthio, monoalkylamino and dialkylamino.

17. A compound according to any of claims 1 to 15 wherein R_4 is selected from NR_7R_8.

18. A compound according to claim 16 or 17 wherein R_4 is NR_7R_8 and R_7 is hydrogen.

19. A compound according to claim 18 wherein R_4 is NR_7R_8 and R_8 is hydrogen.

20. A compound according to claim 16 or 17 wherein R_4 is NR_7R_8 and R_8 is substituted or unsubstituted alkyl.

21. A compound according to any of claims 1 to 15 wherein R_4 is selected from NR_7R_8, $NR_7NR_8COR_9$, $NR_7NR_8CO_2R_9$, $NR_7CO_2R_8$, $NR_7NR_8CONR_9R_{10}$, $NR_7NR_8SO_2R_9$, $NR_7NR_8CSNR_9R_{10}$, $NR_7NR_8R_9$ and NR_7COR_8.

22. A compound according to claim 21 wherein the R_7 substituent of the R_4 group is hydrogen.

23. A compound according to any of claims 1 to 15 wherein R_4 is an NR_7R_8 group and the R_7 and R_8 groups together form a ring to produce a saturated or partially unsaturated, substituted or unsubstituted 5-, 6- or 7-membered cyclic amino group optionally containing one or more additional heteroatoms.

24. A compound according to claim 23 wherein the heteroatoms of said cyclic amino group are selected from N and O.

25. A compound according to claim 23 wherein the cyclic amino group is selected from pyrrolidinyl, pyrrolidinonyl, piperidinyl, piperazinyl and morpholinyl groups.

26. A compound according to claim 1 which is selected from (2R)-2-(1-Hydroxy-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, 2-(3-(1H-Imidazol-1-yl)propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, (2RS)-2-(1-Hydroxy-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, 2-(3-Hydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, 3-Methyl-N-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)butanamide, Methyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate, 2-(2-(1H-Imidazol-4-yl)ethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, (2RS)-2-(2,3-Dihydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, (2R)-2-(2-Hydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, 2-(2-Hydroxyethylamino)thieno[3,2-d]pyrimidin-4-yl 3-methyl-2-thienylmethanone, 2-Chloroethyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate, (2S)-2-(1-Hydroxy-2-propylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, 2-(3-(1H-Imidazol-1-yl)propylamino)thieno[3,2-d]pyrimidin-4-yl 3-methyl-2-thienylmethanone, N-(2-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)cyclohexylcarboxamide, Ethyl 4-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-ylamino)butanoate, 2-(2-Pyridylmethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, (2S)-2-(2-Hydroxypropylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, N-Allyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea, N-(2-(4-(2-Thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)acetamide, 2-(Tetrahydrofuran-2-ylmethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, N-Benzyl-N'-(2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)urea, 2-(2-Hydroxyethylamino)thieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone, Benzyl (2-(4-(2-thienylcarbonyl)thieno[3,2-d]pyrimidin-2-yl)aminoethyl)carbamate and 2-Aminothieno[3,2-d]pyrimidin-4-yl 2-thienylmethanone.

27. A compound according to any one of claims 1 to 26, or a pharmaceutically acceptable salt thereof, for use in therapy.

28. The use of a compound according to any of claims 1 to 26 or a pharmaceutically acceptably salt thereof in the manufacture of a medicament for the treatment or prevention of a disorder in which the blocking of purine receptors may be beneficial.

29. A method of treating or preventing a disorder in which the blocking of purine receptors may be beneficial comprising administration to a subject in need of such treatment an effective dose of a compound as set out in any one of claims 1 to 26 or a pharmaceutically acceptable salt thereof.

30. A use or method according to claim 28 or 29 wherein the disorder is caused by the hyperfunctioning of purine receptors.

31. A use or method according to any one of claims 28 to 30 wherein the purine receptors are adenosine receptors.

32. A use or method according to claim 31 wherein the adenosine receptors are A_{2A} receptors.

33. Use of a compound as set out in any one of claims 1 to 26 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment or prevention of movement disorders in a subject.

34. A method of treating or preventing movement disorders comprising administration to a subject in need of such treatment an effective dose of a compound as set out in any one of claims 1 to 26 or a pharmaceutically acceptable salt thereof.

35. A use or method according to claim 33 or 34 wherein the movement disorder is Parkinson's disease.

36. A use or method according to claim 35 for treatment of drug-induced Parkinsonism, post-encephalitic Parkinsonism, Parkinsonism induced by poisoning or post-traumatic Parkinson's disease.

37. A use or method according to claim 33 or 34 wherein the movement disorder is progressive supernuclear palsy, Huntingtons disease, multiple system atrophy, corticobasal degeneration, Wilsons disease, Hallerrorden-Spatz disease, progressive pallidal atrophy, Dopa-responsive dystonia-Parkinsonism, spasticity, Alzheimer's disease or other disorders of the basal ganglia which result is dyskinesias.

38. A use or method according to any one of claims 33 to 37 wherein the compound of formula (I) is in combination with one or more additional drugs useful in the treatment of movement disorders, the components being in the same formulation or in separate formulations for administration simultaneously or sequentially.

39. A use or method according to claim 38 wherein said additional drug(s) useful in the treatment of movement disorders is/are a drug useful in the treatment of Parkinson's disease.

40. A use or method according to claim 38 or 39 wherein the or one of the additional drugs is L-DOPA.

41. A use or method according to any one of claims 28 to 32 wherein said disorder is depression, acute or chronic pain or a cognitive disorder.

42. Use of a compound as set out in any one of claims 1 to 26 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for neuroprotection in a subject.

43. A method of neuroprotection comprising administration to a subject in need of such treatment an effective dose of a compound as set out in any one of claims 1 to 26 or a pharmaceutically acceptable salt thereof.

44. A use or method according to claim 42 or 43 wherein said medicament or said method is for neuroprotection in a subject suffering from or at risk from a neurodegenerative disorder.

45. A use or method according to claim 44 wherein said neurodegenerative disorder is a movement disorder.

46. A use or method according to claim 45 wherein said movement disorder is a disorder as set out in claim 35, 36 or 37.

47. A use or method according to any one of claims 28 to 46 wherein the subject is human.

INTERNATIONAL SEARCH REPORT

Internati Application No
PCT/GB 00/02517

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D495/04 C07D491/04 A61K31/505 A61P25/14
//(C07D495/04,333:00,239:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, EPO-Internal, BEILSTEIN Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 05139 A (ABBOTT LAB) 13 February 1997 (1997-02-13) claim 1 ---	1-47
A	STRAPPAGHETTI G ET AL: "Adenosine receptors: synthesis, structure-activity relationships and biological activity of new 6-amino purine derivatives" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY.CHIMICA THERAPEUTICA,FR,EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, vol. 33, no. 6, 1 June 1998 (1998-06-01), pages 501-508, XP004143107 ISSN: 0223-5234 table I -----	1-47

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 October 2000	06/11/2000

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Internati Application No
PCT/GB 00/02517

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9705139 A	13-02-1997	CA 2227695 A	13-02-1997
		EP 0842178 A	20-05-1998
		JP 11510171 T	07-09-1999
		US 6001849 A	14-12-1999